THE DYSENTERIC DISORDERS

THE

Dysenteric Disorders

The Diagnosis and Treatment of Dysentery, Sprue, Colitis and other Diarrhœas in General Practice

By

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2nd Edition

WITH AN APPENDIX
by

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With 9 Colour, and 14 Black and White Plates, and 108 Illustrations in the Text



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DEDICATED

TO

My Medical Colleagues and the Nursing Staff of the Hospital for Tropical Diseases, London

PREFACE TO THE FIRST EDITION

"Behold, O Lord, for I am in distress, my bowels are troubled."
Lamentations, **i, 20.**

"My liver is poured upon the earth."
Lamentations, **ii, 11.**

DURING the last thirty years it has become more generally recognized that many forms of disease of the bowels exist and are caused by entirely different agents, although the outward signs and symptoms may closely resemble one another.

Many of the organisms responsible have now been classified and studied extensively; their life-histories have been worked out and therapeutic agents which act directly upon them discovered. The present is therefore an opportune occasion to digest and review the existing knowledge on the dysenteric diseases and to assess in some measure the value of the different forms of treatment which have been elaborated.

It is felt that there is a real need for a comprehensive account of the dysenteries, the various forms of colitis, sprue, helminthic diseases, and the different diarrhœas which form such a complex assembly in general and consulting practice. In addition to dysenteries, there are many affections of the colon—the various and enigmatical forms of colitis, by no means peculiar to warm countries—which bulk largely in practice and upon which a great deal of more accurate information is much to be desired.

It is with the aim of stimulating research [illegible]

has been taken in hand. Much of the information which is made available in this book exists already widely scattered throughout the literature.

The differential diagnosis of the various forms of colitis from the better known forms of dysentery is one which confronts the practitioner in the tropics almost daily; but it is necessary to state that this book, although it embraces a number of conditions which are generally regarded as "tropical," has not been undertaken solely from that specialized viewpoint; rather has it been written from the standpoint of general medicine. In hardly any

other branch of the medical art are the niceties of differential diagnosis so important. It is, for instance, a gross error to diagnose and treat acute bacillary dysentery, or acute colitis, as intestinal amœbiasis, and therefore to inject large doses of emetine—a particularly toxic drug

Having been engaged more or less continuously for over thirty years in the study of this subject from the bacteriological, pathological and clinical aspects, I have drawn largely from my own records; indeed I have endeavoured to make this book the outcome of a life's study As an example, the numbers of cases studied at the Hospital for Tropical Diseases in the preparation of the clinical section of this work are as follows —

Chronic bacillary dysentery	107	
Amœbic dysentery (definitely diagnosed)	535	
Sprue	423	(males 265, females 158)
Ulcerative colitis	42	
Polypus	14	
Polyposis	4	
Mucous colitis	116	
Intestinal tuberculosis	13	
Intestinal bilharziasis	15	
Gall bladder diseases	30	
Duodenal ulcer	40	
Appendicitis	73	
Diverticulitis	17	
Gastric ulcer	12	

The more technical aspects, the zoological description of the intestinal protozoa and bacteria, the methods employed in their

Assistant, Mr W J. Muggleton, with whom I have been closely associated for the past twenty-eight years.

My best thanks are also due to Drs W E Cooke, F R C S I., and J. N Strauss, M.R.C P, for many kindly suggestions in the preparation of this work

PHILIP MANSON-BAHR.

149, Harley Street,
London, W.1.
January, 1939

PREFACE TO THE SECOND EDITION

SINCE the publication of this work three years ago serious and vital events have taken place which have disturbed and too often barbarously checked the ordered progress of scientific thought and work Though the horrors of mechanised warfare have changed the tenets and habits of men, they have in no way altered the inherent nature of pathogenic organisms and the ravages of disease These remain as ever inevitable accompaniments of war and a menace to mankind, so that it is only reasonable to expect that dysenteric conditions will play as great a part in the outcome of this world conflict as they did in the similar catastrophe a quarter of a century ago

As I have been actively engaged in the investigation and treatment of the dysenteries since 1909, it fell to my lot to benefit by an unexampled experience of these diseases in the Middle East during the whole period of the last war. The results of these laboratory investigations and their clinical application in times of war and peace set forth in these pages, were prefaced by special researches undertaken on dysentery and sprue in Fiji and Ceylon during the years 1909–1913

Though no vital alterations have been made in the general arrangement of the book, mention is made of the many improvements effected in treatment, especially the introduction of sulphaguanidine in bacillary dysentery. In view of the recent new light on the ætiology of the sprue syndrome and the relationship of this interesting symptom-complex to the steatorrhœas and fat absorption, a new chapter on pellagra has been inserted, a better understanding of the complexities of this nutritional disorder having shed much light upon the group of diseases with which it has many aspects in common

The demand for this second edition has been evoked by the present cataclysm as well as by the necessity of including many advances in ætiology, diagnosis and treatment which in the interval have become available It is hoped that, by their timely publication in an easily-assimilable form, the volume may become helpful to all in the armed forces or medical services at home or abroad who may be called upon to treat the many varied and puzzling phases of the dysenteric disorders With this end in view I have tried by every means in my power to make this revision as complete as possible. In so doing I have been encouraged by the generous reception afforded by the profession to the first edition of the work.

PHILIP MANSON-BAHR.

149, Harley Street, W 1.
February, 1942.

CONTENTS

LIST OF PLATES

INTRODUCTION

By J. Johnston Abraham, C B E , D S O , F.R C S
Author of "The Surgeon's Log," etc

This is a book that needed to be written, and the wonder is that such a work had not been attempted before Probably the reason is that it required an experience both of European and tropical diseases of the alimentary tract such as few possess, coupled with an industry in collecting and tabulating what has been written on the subject in scattered papers in several languages that would daunt all but the most intrepid. Dr Manson-Bahr possesses both the experience and the courage to tackle this task He has done so in the book before us, and the profession accordingly owes him a debt of gratitude

The history of the differentiation of the dysenteries is an important one. The dysentery amœba was discovered by Losch in 1875, and the dysentery bacillus by Shiga in 1898 This time-lag has been unfortunate, since it has produced a general belief in the minds of many that all dysenteries in the tropics must be amœbic, while it is still not fully recognized that bacillary dysentery is of the two the more widespread and important

This was especially so in the Great War. It was bacillary dysentery and not the Turk that drove us out of Gallipoli. With proper precautions we should never have had an epidemic of dysentery there, for the disease is a fly-borne one, as Manson-Bahr

Luckily, by the time the remnants of the troops came back to Egypt, the mistake had been discovered, and throughout the Sinai campaign the elaborate precautions taken to prevent fly-breeding protected the great base camps from any further outbreak This was a very remarkable feat when one considers that at Kantara on the Suez Canal there were one hundred and twenty thousand men with no sanitation except field latrines, and that British, Colonial, Indian and European *troops were all camping*

DYSENTERIC DISORDERS

CHAPTER I

METHOD OF PROCEDURE IN INVESTIGATING A CASE OF DIARRHŒA OR DYSENTERY

In the complete investigation of the causes of acute and chronic diarrhœa and the many diverse conditions which border upon dysenteric disorders, it is necessary to bring into play most of the resources at the disposal of the modern physician, elucidation of a case, therefore, requires an extensive knowledge of medicine in general

In Table I will be found a list of the known causes of diarrhœa in adults and children, but to describe all these *in extenso* would entail the compilation of a complete medical textbook. This is far from being the object of the table, which is designed as a means of conveying to practitioner and student the wide range of the subject, and of suggesting details to which his special attention should be directed In Table II are classified the different steps, in due order, which should be undertaken in the investigation of a patient suffering from diarrhœa or dysentery.

The special diseases with which this book deals are those which in some form or other, fall into the dysenteric syndrome, and these demand special laboratory methods to establish a diagnosis. The main interest of the book centres round the subject of the dysenteries and colitis, and within it diagnosis and treatment are handled at some length with the idea of assisting the specialist, practitioner and student to obtain an insight into an admittedly complex subject

TABLE I

CLASSIFICATION OF THE CAUSES OF DIARRHŒA

IN ADULTS

Primary diarrhœa
- Diet
- Constipation
- Changes of climate, or weather
- Irritants taken with food—mushrooms, mercury, arsenic, or ptomaine poisoning

Alterations of intestinal secretion or absorption
- Acute and chronic dyspepsia (gastrogenous), pancreatogenous diarrhœa, cholecystitis
- Idiopathic steatorrhœa (cœliac disease), non-tropical and tropical sprue, hill diarrhœa.
- Nervous diarrhœa

alongside one another None the less, the military mind still clung to the idea that amœbic dysentery would be found endemic in [illegible]

A knowledge of the dysenteries is of increasingly great diagnostic importance to all practitioners of medicine both at home and in the tropics For, as the time-distance between countries decreases and people travel more and more, the risk of infection mathematically increases, and we may expect to see more and more diseases, once confined to the tropics, in every-day practice in Europe.

There is, however, no likelihood of amœbic dysentery ever becoming endemic in the British Isles, owing to the excellence of our sanitary arrangements, but a knowledge of the dysenteries is essential if one is to understand the extent and treatment of colitis, enteritis and other similar abdominal diseases, and the wonders that can be done by the proper utilization of the modern *drugs now at our disposal should be familiar to all*

Dr Manson-Bahr's treatise is a mine of information on these subjects.

TABLE II

METHOD OF PROCEDURE IN THE INVESTIGATION OF A PATIENT SUFFERING FROM DIARRHŒA*

1. History.

Features in history indicating possible causes
Sharpness of onset or chronicity
Dietetic habits
Previous residence in the tropics, noting particularly geographical distribution of intestinal disease
Liability to chills

2. General Examination —Paying special attention to —

(a) *Skin* Petechiæ (septic endocarditis)
Texture (endocrine disease)
Pigmentation (kala azar, Addison's disease, arsenic, etc)
(b) *Neck* Thyroid (hyper- or hypothyroidism)
(c) *Lungs* Tuberculosis, compression signs as in amœbic abscess of liver, pulmonary abscess
(d) *Cardio vascular* Congestion, septic endocarditis
(e) *Tongue* Sprue, pellagra, idiopathic steatorrhœa, syphilis, gastrogenous diarrhœa
(f) *Central Nervous System* Lesions causing incontinence—e g tabes, etc
(g) *Glands* Inguinal bubo if suggestive, Frei Hoffmann test in lymphogranuloma, leukæmia
(h) *Abdomen* Palpation
Masses—carcinoma of colon, diverticulitis, bilharziasis, amœbiasis, tuberculoma, actinomycosis, intussusception
Doughy (tuberculosis)—sprue or steatorrhœa
Enlarged spleen or liver—cirrhosis, carcinoma, malaria, leukæmia, etc

3. Digital rectal examination.

Carcinoma, piles stricture, 'velvety' feel of ulcerative colitis, chronic rectal amœbic ulcer, stricture of lymphogranuloma
Fæcal impaction

4. Stool examination. — (3 stools should be examined if possible)

(a) Naked eye appearance—Dysenteries, sprue (If suggestive —then fat analysis, occult blood, test meal, glucose curves)
(b) Helminth eggs Bilharzia, ancylostoma, fasciolopsis, heterophyes, etc.
(c) Protozoa Amœbæ, balantidium giardia, coccidium, etc
(d) Charcot-Leyden crystals

5. Blood examination.

Count —sprue anæmia
Parasites —malaria
Serum agglutination —against dysenteries and the Salmonella group
Leucocyte count and differential count of value in amœbiasis and tuberculosis. Eosinophilia in trichinosis, bilharziasis, etc

* This is to be considered as a mere outline containing points which a practitioner should bear in mind on approaching a case

Secondary diarrhœa. Infective conditions

Typhoid and paratyphoid fevers (Salmonella group).

Bacillary dysentery—Shiga, Schmitz, Flexner and Sonne infections.

Cholera

Gærtner and Aertrycke infections

Amœbiasis and amœbic dysentery, balantidiasis, giardiasis, flagellate diarrhœa coccidiosis, malarial dysentery, leishmanial dysentery.

Trichinosis, bilharziasis, fasciolopsis, heterophyes and other worm infections

General infections

Endocarditis, septicæmia and pulmonary tuberculosis

Diseases of intestines

Carcinoma

Tuberculosis

Syphilis

Actinomycosis

Diverticulitis

Chronic cicatrizing enteritis (Crohn's disease).

Peritonitis

Appendicitis

Hæmorrhoids

Blood diseases

Henoch's and other forms of purpura.

Chronic circulatory disturbance

Portal congestion

Cirrhosis of the liver

Chronic heart and lung disease

Toxic

Hyperthyroidism (thyrotoxicosis)

Chronic alcoholism

Uræmia

Lardaceous disease.

Avitaminosis

Pellagra and prepellagrous conditions

Special types of diarrhœa

Ulcerative colitis

Muco-membranous colitis

Polyposis

Polypus.

Stercoral ulceration

Foreign body in rectum.

IN CHILDREN

[illegible] (summer diarrhœa)

[illegible]

[illegible]

[illegible]

Amœbic dysentery

Cœliac disease.

Intussusception.

Polypus.

Thus in the full elucidation of a case of dysenteric disease, or of chronic diarrhœa, nearly all the ancillaries of medical practice may

investigation which actually still remain of most value, and which are always at his command

6. **Urine.**—Casts, etc—uræmia (If suggestive, blood urea) Porphyrinuria in pellagra and sprue
7. **Wassermann.**—Tabes Rectal stricture.
8. **Sigmoidoscopy.**—Numerous lesions diagnosed thereby :—dysenteries, carcinoma, polypus and polyposis, ulcerative colitis, etc.
9. **Barium enema.**—Growths, colitis of different kinds
10. **Barium meal**—Appendicitis, diverticulitis, stenosis, stricture, tumour, regional ileitis (Crohn's disease).

There are dysenteriform diseases in which the clinical picture is so

In many instances, from the actual physical examination and appearances of the patient no positive information can be elicited. This is often the case in amœbiasis and in the milder forms of bacillary dysentery Special attention must be paid to the presence or absence of wasting and to the general appearance of the abdomen, whether sunken, navicular, swollen or turgid

Other important points in the examination of the abdomen are the presence or absence of meteorism, areas of tenderness discovered on deep pressure, a sensation of spasticity of the colon, or actual thickening of its walls The size and consistency of the liver discovered by deep percussion or palpation are important, as is also discomfort directed towards the gall-bladder. The colouring and general features of the complexion and texture of the skin must also be noted.

After the physical examination of the patient comes the positive information derived by proctoscopy or sigmoidoscopy, by which means a view of the mucous membrane may be obtained At the same time the all-important microscopical examination of the fæces must be undertaken—an extensive and specialized subject—the presence or absence of inflammatory cells and blood and the character of the non-digested contents being duly noted. The search for intestinal protozoa or the eggs of helminths should be carried out with a comparatively low-power lens (i e $\frac{1}{6}$) before proceeding to the more elaborate bacteriological culture of the stools.

Finally, with a due sense of proportion as to the value of information thus obtained, the radioscopic examination of the bowel should be conducted. Probably much more accurate knowledge is vouchsafed

tests have each their appropriate place.

The levator ani muscle itself may also be divided into three portions —

1 The *iliococcygeus*, arising from the ischial spine and from the posterior part of the white line It is inserted into the coccyx and the ano-coccygeal raphé It is usually only represented by fibrous tissue and may be regarded as a degenerating muscle whose primary function —flexion of the tail—has been lost

2 The *pubococcygeus*, which arises from the back of the os pubis and from the anterior part of the obturator fascia, the fibres are directed backwards horizontally along the rectum at a higher level than the puborectalis

3. The *puborectalis* arises from the back of the symphysis pubis and forms the upper part of the triangular ligament From this origin the fibres pass backwards and also downwards around the lower and lateral aspect of the rectum, meeting with fibres from the opposite side behind the anal canal, so forming a powerful loop which slings the ano-rectal junction to the symphysis

The *longitudinal muscle* of the anal canal is a prolongation of the external muscular coat of the rectum surrounding the anal canal At the upper end of this canal it at once becomes fibromuscular, blending in its posterior half with the puborectalis, and in its anterior half with the external sphincter ani profundus, and there takes its shape in the formation of the *ano-rectal ring*

The *sphincter ani externus subcutaneus* is easily palpated and recognized in its whole extent as a round or elliptical band situated at the [illegible] it one quarter [illegible] there is en- [illegible] to an eighth [illegible] This separates the muscle from the more easily recognized lower and rounded edge of the internal sphincter, which itself reaches to within a quarter of an inch of the anal margin The sphincter ani externus subcutaneus is the only portion of the external sphincter which is subcutaneous and is directly palpable throughout The lower border of the internal sphincter can be palpated as the rounded upper boundary of the intermuscular septum encircling the anal canal It extends below the muco-cutaneous junction to within a quarter of an inch of the anal margin

The ano-rectal ring is situated at the junction of the anal canal and rectum It is found to be a composite fibromuscular band composed of the upper portion of (*a*) the internal sphincter, (*b*) the longitudinal muscle, (*c*) the puborectalis, and (*d*) the external sphincter ani profundus muscles It should be possible, by withdrawing and inserting the palpating finger with pressure at this point, to identify this ring with precision The posterior half of the ring is more easily defined because of the prominent string-like fibres of the puborectalis portions of the levator ani The puborectalis, if followed forwards and upwards from behind with the rectal palpating finger can be traced leaving the

CHAPTER II

THE EXAMINATION OF THE BOWEL WITH SPECIAL REFERENCE TO SIGMOIDOSCOPY

WITH the great majority of patients it becomes necessary to undertake a local examination of the bowel This is especially the case when complaint is made of symptoms referable to the rectal canal, and even in cases of genuine dysentery It should always be done unless the diagnosis has been rendered absolutely certain by the recognition of the causative parasite in the stools It cannot too strongly be emphasized that grave mistakes are bound to occur unless a local inspection of the bowel itself is made, and it is obvious that by no other means can malignant growths in their early stage be recognized and dealt with adequately The patient may seek advice solely on account of piles, but the external appearance of hæmorrhoids may be only a warning sign of a more severe pathological lesion higher up the intestinal tract.

There are several methods of examining the bowel For the diagnosis of hæmorrhoids, anal fissures, and fistulæ, the local examination of the rectum with a suitable proctoscope is sufficient, but for any more extensive investigation a sigmoidoscope is necessary. Digital examination of the rectum should never be neglected This is most important from the viewpoint of the practitioner.

IMPORTANT POINTS IN THE SURGICAL ANATOMY OF THE ANUS AND RECTAL CANAL

E T C. Milligan and C N. Morgan, in their study of the surgical anatomy of the anal canal, have laid stress on the fact that the various musculatures of the bowel can and should be palpated and recognized The external sphincter of the anus is a trilaminar muscle which, with the puborectalis portion of the levator ani, forms a strong muscular cylinder encircling the longitudinal muscle, the internal sphincter ani, and the anal canal The three layers are named, from below upwards, 1, the sphincter ani externus subcutaneus, 2, the sphincter ani externus superficialis, 3, the sphincter ani externus profundus The first and third portions are annular muscles not attached to the coccyx; the second portion is elliptical and is attached to the coccyx. The second and third parts encircle the longitudinal muscle and the internal sphincter ani.

modification of Kelly's short rectal tube It should be warmed, well lubricated and gently introduced until the extremity has passed the sphincters The obturator is then removed and, by means of a good [illegible]

Examination with the Sigmoidoscope

Indications for sigmoidoscopy may be summarized as follows:—

1 Complaint of rectal pain, tenesmus, chronic diarrhœa, mucopurulent or blood-stained stools

2. [illegible]

3 [illegible]

4 [illegible]

5 [illegible]

[illegible]

To very nervous and hysterical people, and very sensitive women, a general anæsthetic may have to be given.

It is generally recognized that in practised hands accidents are very rare indeed and R Bensaude, the well-known author of monographs [illegible]

[illegible] in position, is situated one inch from the anterior end of the instrument. By an ingenious arrangement the lamp may easily be removed for cleansing

In order to insert the instrument with comfort, an obturator is provided, which is removed directly the muscular region of the sphincters is passed. The lamp is then introduced, the eye-piece adjusted, and the further passage of the instrument controlled by sight. A smaller modification of the sigmoidoscope, the proctoscope, which is some 15 cm. in length, can be used for the inspection of the rectal canal.

Before using the sigmoidoscope, the operator must assemble the instrument and see that everything is in order, especially must he test the electric lamp, for failure in illumination at the critical

ano-rectal ring on each side of the anal canal to be inserted into the posterior surface of the pubic bones near the symphysis pubis.

The *sphincter ani internus* can only be recognized apart from other sphincter muscles at its lower edge near the anal margin. It lies immediately under the mucosa and is palpated along almost the whole length of the anal canal On withdrawing a long tubular rectal speculum from the distended rectum to the anal canal, the ano-rectal ring contracts as the end of the speculum reaches the junction, and a narrow ring of mucous membrane appears The highest portion of the internal hæmorrhoidal plexus lies just above the ano-rectal ring

Examination of the Rectum

Special preparation of the patient is not necessary for the local inspection of the rectum, as this viscus is usually empty; if fæces are present it suffices to have them removed by a simple enema

The posture most generally adopted for the examination of the patient is the left lateral The buttocks are raised at the edge of the couch, with the left elbow or arm placed behind the head, the chest resting flat upon the couch and the knees well drawn up. Sometimes it is advantageous to place a sandbag under the left hip This left lateral position is the most comfortable and least embarrassing when it is necessary to examine patients in the consulting room Should the patient be very stout or particularly muscular, the adoption of the knee-elbow position usually makes examination much easier. Before inserting any instrument, the external parts must be carefully examined, the condition of the skin noted, and search made for orifices of fistulæ The anal margins should then be gently separated with the fingers to ascertain if any fissure is present, and digital examination is continued with the first finger suitably lubricated. Vaseline is, as a general rule, more satisfactory than glycerin, which is apt to cause pain The examining finger, covered by a thin finger-stall, will cause

any further abnormality be present It is necessary to note that internal piles usually *cannot* be felt, nor their extent estimated by means of digital examination Many mistakes are made by a too rigid

heat They should be cleansed with spirit The eye-pieces require special care. Great help is obtained from a special magnifying eye-piece, such as Wolfe's, which magnifies two diameters (at 30 cm) and which is the pattern the author prefers. For the study of the finer lesions in the bowel, and especially for the recognition of small amœbic ulcers, a magnifying eye-piece is absolutely necessary Fogging of the glass of the eye-piece is prevented by warming before use, or lightly smearing with glycerin

Anatomical considerations.—Inspection of the rectum and the sigmoid loop would be very easy were the rectum a perfectly straight tube, but as it is not, the examiner must make himself familiar with the arrangement of the parts in order to guide the instrument skilfully When the pat
presents its pe
forward, and
antero-posterior
variable

The interior of the bowel is not entirely smooth, for immediately above the sphincter there is a series of longitudinal folds known as the columns of Morgagni The junction of the sigmoid flexure with the rectum is situated about 11–13 cm. from the anus The form of this loop may be compared schematically to the two arms of a V reversed so that in no case is it possible to see beyond 32–35 cm from the anus

The normal appearance of the mucous membrane and bowel—In the normal subject the mucous membrane has a uniform rose or rose-red

mucosa (Figs 3, 4, 5, 6)

The region of the ampulla is furnished with valves At a distance of 7 cm from the anus two valves cross each other at right-angles, the first of these is known as the valve of Houston, the second as that of Nélaton, or the coccygeal valve In 28 per cent of normal people a third valve exists, the superior sacral valve At 11–14 cm, the recto-sigmoid sphincter marks the entrance into the pelvic colon This is more commonly known as the sphincter of O'Beirne and it is always

... which is sometimes difficult to surmount. The sphincter having been passed, the entrance into the sigmoid loop is seen to be marked by transverse folds At 15–20 cm from the anus a region is reached where will be seen pulsations conducted from the internal iliac artery, and this appearance is most characteristic. Between 25 and

moment is extremely annoying In these small electric bulbs, such failure may be brought about by trifling causes, which must be discovered The strength of the current can best be tested by putting the terminals on the tongue, when the characteristic sensation is produced Very often the defect is in the holder of the bulb itself, the *wires of which may be freed by a pin*

Other instruments necessary in sigmoidoscopical examination are :—

1

2

bacteriological examination

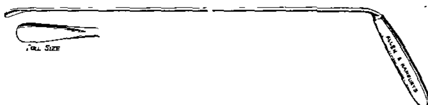


Fig. 1.—The author's long-handled Volkmann spoon for obtaining material from ulcers through the sigmoidoscope for microscopic examination.

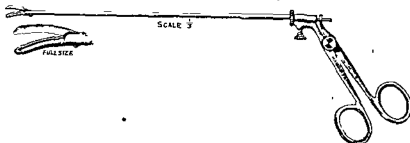


Fig 2.—Biopsy forceps for use with the sigmoidoscope.

3 A long-handled spoon on the principle of the Volkmann spoon, which the author employs to obtain scrapings of dysenteric ulcers for microscopic examination. (Fig 1.)
4. Forceps for obtaining pieces of tissue from the bowel for microscopic examination or biopsy * (Fig. 2.)
5. An insufflator for blowing in medicated substances.
6 A snare for removal of polypi (Lockhart-Mummery's type).

The tube and obturator should be sterilized in boiling water before use, but the other parts of the sigmoidoscope should not be subjected to

* The author favours the pattern manufactured by Vann Bros , 63, Weymouth Street, London, W

in the fundus oculi, and this can only be satisfactorily performed by

of each disease.

underlying the mucosa, and there may be venous varices simulating ecchymoses When the hæmorrhoids are inflamed, a hæmorrhagic rectitis is produced and the patient may appear pale and cadaverous

Preparation of the patient.—For a satisfactory examination it is essential that the lower bowel should be entirely free from fæces, and to ensure this practitioners adopt various methods It is seldom possible to examine a patient suitably without some form of preparation, unless the bowels have been naturally well emptied just previously Methods of cleansing the bowel vary according to the condition of the patient, whether constipated, diarrhœic, or normal Usually it is necessary to inject a pint or more of hot water three to four hours before the time fixed for the examination, and to continue lavage till the effluent is perfectly clear. In cases of severe constipation strong cathartics must be used with caution, because their action may be continued during the examination, flooding the bowel with liquid fæces

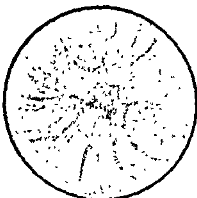
Not later than 2 p.m. on the day before, the patient should be given ½–¾ oz. of castor oil. and lavage of the rectum should be performed on the morning of the examination Should the patient be suffering from diarrhœa, then the preliminary aperient must be omitted 5–15

It is essential that the preparation should be conducted in a hospital or some institution where there are trained nurses because, if left to themselves, patients invariably take the enema too late The patient must always be instructed to pass urine immediately before examination.

Some authorities prefer to examine the bowel without any preliminary preparation, claiming that the mucous membrane will then best be seen in its natural state; this is the practice at St. Mark's Hospital, in London.

32 cm fall the limits of the ascending loop of the sigmoid, an well-marked folds of mucous membrane are encountered

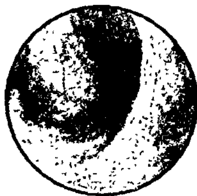
In performing sigmoidoscopy the operator should take note normal arrangement of the blood-vessels which run parallel wi



2, Normal rectum in the region of the internal sphincter, showing the pitted appearance due to the openings of the ducts of anal glands.



4, Normal rectum at 7 cm. from an Houston's valves.



5, Normal rectum upper portion at 10 cm. from anus, showing appearance of branched blood-vessel on surface of mucosa.



6, Entrance of sigmoid at 13 cm., recto-sigmoid sphincter.

Figs. 2-6.—Normal appearances of rectum and sigmoid as seen by sigmoid *(Partly after Bensaude)*

folds of the mucous membrane *In inflammatory states of the* membrane itself the contour of these vessels may be obscured

in the fundus oculi, and this can only be satisfactorily performed by a magnifying eye-piece

The characteristic and diagnostic appearances of the various pathological conditions described will be found in the appropriate sections of each disease

[illegible]

underlying the mucosa, and there may be venous varices simulating ecchymoses When the hæmorrhoids are inflamed, a hæmorrhagic rectitis is produced and the patient may appear pale and cadaverous

[illegible]

usually hypertrophied, giving a crenated appearance

Preparation of the patient.—For a satisfactory examination it is essential that the lower bowel should be entirely free from fæces, and to ensure this practitioners adopt various methods It is seldom possible to examine a patient suitably without some form of preparation, unless the bowels have been naturally well emptied just previously Methods of cleansing the bowel vary according to the condition of the patient, whether constipated, diarrhœic, or normal Usually it is necessary to inject a pint or more of hot water three to four hours before the time fixed for the examination, and to continue lavage till the effluent is perfectly clear In cases of severe constipation strong cathartics must be used with caution, because their action may be continued during the examination, flooding the bowel with liquid fæces

Not later than 2 p m on the day before, the patient should be given ½–¾ oz of castor oil, and lavage of the rectum should be performed on the morning of the examination Should the patient be suffering from diarrhœa, *then the preliminary aperient must be omitted* 5–15 minims of tincture of opium being given half to one hour beforehand If the diarrhœa be very severe, an injection of ¼ gr of morphia is much more satisfactory. As a routine the author finds it advantageous to dull sensation by giving 1–2 gr of luminal half an hour before instrumentation, which then becomes practically painless.

It is essential that the preparation should be conducted in a hospital or some institution where there are trained nurses because, if left to themselves, patients invariably take the enema too late The patient must always be instructed to pass urine immediately before examination

Some authorities prefer to examine the bowel without any preliminary preparation, claiming that the mucous membrane will then best be seen in its natural state, this is the practice at St. Mark's Hospital, in London

The examination itself is best performed on a properly constructed table. If such a table is not procurable, an ordinary operating table, provided with lithotomy stirrups, is a useful substitute.

Position of the patient.—The position in which the patient is placed for sigmoidoscopy is very important. Undoubtedly the genupectoral position is the one most favourable from the operator's point of view, as the rectum and pelvic colon then fall more or less into a straight line, and the instrument can in most cases be inserted directly into the bowel without the aid of inflation. But in practice this position has not been found acceptable to the majority of British patients. Moreover, in elderly people and those who are cachectic or otherwise in bad health, it is apt to cause giddiness and faintness. When a special sigmoidoscope table is provided, it is possible to arrange the patient lying on his abdomen with his head directed towards the floor. This position has the same advantages as the genupectoral. The dorsal posture, with the knees raised, i.e., the lithotomy position, is the one most usually employed, being the most convenient for the patient. It has the disadvantage that sometimes considerable inflation of the bowel is required to enable the sigmoidoscope to be passed, and also that considerable skill is often needed to direct the instrument round the various bends. The Sims dorso-lateral position, where the patient is placed on his right side with the buttocks elevated on sandbags, facing the operator, and with the knees drawn up, has the advantage of being much less fatiguing, and is therefore more suitable for prolonged examination or where the patient is in a feeble state of health. It is the position most favoured by the patient. The vertical position of Granville S. Hanes, in which the patient is literally standing on his head, has been used for high sigmoidoscopy, especially in America, but it is quite unsuited for any but the most robust.

Technique. [illegible]

a suppository [illegible]
a fissure 20 c[illegible]
into the rectu[illegible]
in warm wate[illegible]
it must be remembered that the anus is extremely sensitive to heat. The tube itself should be well lubricated with vaseline or, better still, [illegible]

light inserted and further passage through the lumen of the bowel guided solely by sight. In the genupectoral position the passage is easy and insufflation is not required, but in the dorsal and lateral positions inflation is essential; the necessary pressure on the bulb should be made by the operator himself, who should instantly release it should the patient complain of acute pain. After passing the sphincter region, when the patient is in the lithotomy position, the instrument is held horizontally, and then directed upwards and backwards in the direction of the rectal ampulla. At 11 cm it must again be directed in a horizontal direction so as to find the entrance of the pelvic colon This loop is not usually situated medially, and is directed towards the left more often than to the right Again the direction should be at first horizontal and then vertical, until the entrance to the loop is secured. This is by no means always easy, and frequently the operator has to withdraw the instrument for a short distance, at the same time

the ball, looks for an opening space into which he may plunge

When the descending branch of the pelvic loop is penetrated, the operator must manipulate the instrument and insufflate the bowel It is necessary always to keep the lumen of the intestine in the centre of the field of vision as the instrument is advanced This is as far as one can safely proceed, and at that stage it should be possible to palpate

examiner can observe minutely the folds of mucous membrane as they present themselves More important observations upon the position

In order to cleanse the bowel, some pledgelets of cotton-wool are introduced in the crocodile-forceps, and they may also be employed to remove an excess of fluid or liquid fæces. Water syphonage can also be adapted and the apparatus may be attached to the nearest tap, this is often extremely useful when the bowel contents are copious and offensive. Besides rendering the lumen of the bowel patent, insufflation has other advantages, it may be employed to delineate the outlines of a tumour or to test the elasticity or otherwise of the mucosa. In normal conditions the natural folds of mucous

The exa
table If
provided

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membrane are rapidly reduced under gentle insufflation and re-form ... ast, when ... the folds ... er force is ... ses pain, thus, in the inflammatory states, sigmoidoscopic examination is more painful than when simple ulcerative lesions are present A certain amount of skill is required in controlling the forces of insufflation, and usually beginners overdo this process, thereby causing unnecessary pain and inconvenience

The distance that can be attained with a sigmoidoscope depends, ...

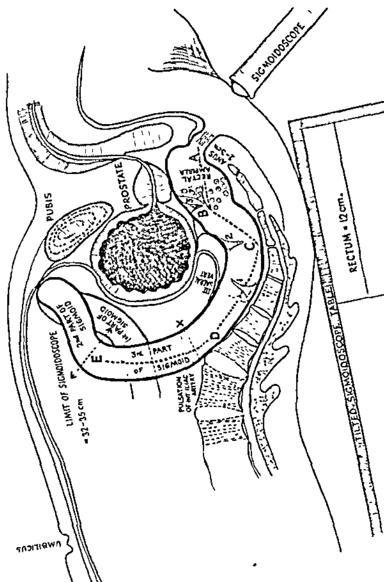
anæsthetic. Where an intestinal tumour can be felt in the abdomen its examination by sigmoidoscopy is most necessary before the surgeon can proceed to laparotomy

Sometimes the walls of the intestines, being abnormally dry and lacking in mucus, cling to the sides of the instrument like the fingers of a glove, sometimes, also, the walls of the bowel become stretched over the upper end of the sigmoidoscope like a drum, and when undue pressure is made by the operator in these circumstances, perforation of the bowel may occur This is specially likely to take place when the bowel wall is weakened or attenuated by a prolonged ulcerative process.

Radiography can be employed to determine the extent to which the instrument has been passed, and it is surprising to see the position in which it may lie in the abdomen, thus demonstrating the variation in the anatomical position of the sigmoid flexure The extremity may even be found in the epigastric region or abutting the lower edge of the liver

The routine employment of the sigmoidoscope should not encourage the examiner to neglect the older methods of examination. The education of the sense of touch is most important There are many instances of small circumscribed cancers of the rectum (8–10 cm above the anus) which can be accurately palpated by the finger and the ...

wall of the rectum, which may be tucked away and hidden in the ... rument ... ls may ... ted ... This



SIGMOIDOSCOPE
PUBIS
PROSTATE
RECTAL AMPULLA
ANUS
A
B
C
D
E
F
X
III SACRAL VERT
RECTUM = 12 cm.
TILTED SIGMOIDOSCOPE TABLE
2nd PART OF SIGMOID
1st PART OF SIGMOID
3rd PART OF SIGMOID
PULSATION OF INT. ILIAC ARTERY
LIMIT OF SIGMOIDOSCOPE = 32-35 cm
UMBILICUS

CHAPTER III

HISTORICAL SURVEY OF THE DYSENTERIES

DYSENTERY, or the "bloudy fluxe" of our forefathers, has been an object of curiosity and study since the earliest times It is now fairly certain that Hippocrates, the Father of Medicine, distinguished it as a disease distinct from other forms of diarrhœa, and that he noted the significance of tenesmus, a symptom which supervened frequently in cases of mortification Aretæus, Celsus, Archigenes, Galen, Cælius Aurelianus and Alexander von Tralles all give somewhat crude clinical descriptions of dysentery Celsus in particular ascribed the "bloudy fluxe" to ulcers in the interior of the intestine which caused the patient to suffer continuously from tenesmus and pain near the anus

These ancient writers, however, appear to have described only sporadic forms of the disease; it was from the fifth century onwards that epidemics were noted in Europe The chroniclers of the period record epidemics of dysentery in France in A D 534 and 538, and again in Northern Europe in A D 760

The infectious nature of the disease was first referred to by Fabricius Hildanus in 1646, shortly afterwards ipecacuanha was introduced from

polluted by the roots of *Serpentaria*

In the middle of the seventeenth century the subject of dysentery figured much in medical writings, especially in those of Sydenham, Morton, and Willis concerning the great epidemic of 1668–72. They first distinguished clearly between blood-stained dysentery stools and

is specially so in the case of internal hæmorrhoids which cannot be felt

appointing, but fallacious Finally, reliance must not be placed upon sigmoidoscopy alone to the exclusion of other methods of examination, such as the microscopic examination of the fæces and palpation of the abdomen

In the following table a summary is given of some of the practical results of routine sigmoidoscopy, to which future reference will be made.

TABLE III —STATISTICS

Number of dysenteric cases examined by sigmoidoscopy in the Hospital for Tropical Diseases, 1920–1935, to ascertain the frequency of stricture in tropical practice 3,068

Stenosis and stricture of rectum (incidence 0 8%)	27
Chronic bacillary dysentery	7
Chronic amœbic dysentery (including pericolic abscess)	5
Ulcerative colitis	2
Tuberculosis of colon	2
Syphilitic stricture	1
Gonorrhœal proctitis	1
Polyposis	1
Lymphogranuloma inguinale	2
Diverticulitis	1
Carcinoma of rectum (post-dysenteric)	5

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[illegible]

with a perpetual purging, at first mucous, and afterwards bloody, and lastly purulent, with intolerable pain and griping of the belly" Bontius ascribed the epidemic to the defilement of the air and drinking-water by the dead bodies of men and animals, and to the water being polluted by the roots of *Serpentaria*

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[illegible]

Pringle had given accurate accounts of dysentery in the English Army, and G Cleghorn in the English Fleet off Minorca. Pringle (1752) fully realized that epidemic dysentery constituted a single entity, and that it was an infectious malady conveyed by the discharges of the patient In 1767 J G Zimmermann wrote a book on the dysentery epidemic he had observed in Switzerland, and gave an accurate description of the clinical varieties of the disease.

During the first half of the nineteenth century the theory still prevailed that dysentery was but one expression of malaria, so that it remained for Cruveilhier, Rokitansky and Virchow, by patient and exact observations, to put the pathological processes of the disease on a more secure basis

The resemblance of dysentery to malaria in its tendency to break out at long intervals in pandemic form, extending over tracts of country, impressed many observers, notably Hirsch (1856), until recent times. Such epidemics were noted in the United States in the years 1749–53, 1773–77, and 1793–98 In France it raged in 1749–50 and again in 1759, especially in the Central and Southern provinces In Switzerland a pandemic occurred in 1659 , in Holland in 1556 and 1624 ; in Belgium in 1891 and in Luxemburg in 1863.

In 1540 dysentery was noted over a large part of England, and again in 1668–72 In Ireland there are records from 1728–30, and it appears that dysentery was associated with typhus in the famine years of 1817–18 and again six years later In Marlborough's days dysentery was so common in Ireland that it was known as the "Country Disease"; and at the siege of Dundalk in 1689 there were 6,000 deaths from this cause In Germany it was widely spread , for instance, in 1676–78 it occurred in Saxony and the Rhine Provinces, and in 1726–28 in Silesia, Saxony, and the Mark of Brandenburg. In Sweden, 1619–52, it raged "over nearly the whole country," and in 1770–75 in nearly every province ; similar conditions were noted in the southern districts of Norway, 1808–10. In Italy there is one instance, in 1787, of an epidemic which spread widely throughout the land.

One of the most extensive and malignant of dysentery pestilences in the central parts of Europe occurred in the years 1834–36. In

famine. The war-pestilence of Athens during the Peloponnesian War has been paralleled by experiences during the nineteenth century.

The Wars of Napoleon 1790–1815, the Crimean War, 1854–55, the Franco-German War, 1870–71, the Russo-Turkish War, 1878–79, the English Campaign in New Zealand, 1860–61—in the Eastern Hemisphere and in the Western—the French occupation of Mexico, the Secession War in the United States, have proved repeatedly that dysentery must be placed with typhoid and typhus among the foremost pestilences of war

Famine and sickness consequent on failure of crops were responsible for dysentery in Ireland in 1800, 1817, 1821, 1826, and 1846–7, in Tobolsk, Russia, in 1863 and in Upper Senegambia, Africa, 1853–55 Smaller outbreaks are recorded in Iceland in 1850, where the disease broke out in consequence of bad food Outbreaks of dysentery tended to occur in prisons, barracks, and institutions of those kinds, and among the poorer classes of the people, and among the rural population rather than the urban

A Survey of the Literature of Dysentery in Tropical Regions

ns was well known in
ards the close of the
drawn to this disease
was appalling

The Spanish Wars and Elizabethan enterprises had secured an enduring heritage for Great Britain in the West Indies, and here, among the negro slaves, the British garrison, and the fleets which cruised the Caribbean Seas, epidemics of dysentery were studied and treated by an almost bewildering variety of remedies In the writings of the naval and military surgeons we find a tendency to differentiate forms of dysentery on purely clinical grounds, but it is to a practising physician, James Grainger, of St Kitts, that credit must be given for distinguishing, in an essay on "The More Common West India Diseases and the Remedies which that Country Itself Produces," (1764), two fundamentally distinct types, in this manner anticipating the East Indian physicians by nearly forty years From the clinical description of West Indian dysentery in "Observations on the Changes of Air and Concomitant Epidemical Diseases in the Island of Barbados," by W Hillary (1759) and "Observations on the Acute Dysentery" by John Rollo (1786) it is safe to assume that the dysentery they had encountered was of the bacillary type

To vapours, humours, and other malign influences put forward as causes of dysentery can be added the "obstructed perspiration" theory advanced by Benjamin Moseley (1787) in "A Treatise on Tropical Diseases and on the Climate of the West Indies" James Trotter, in 1804, describing an epidemic that occurred in the Jamaica fleet after a great hurricane, ascribed its cause to the drenching of

bedding in sea-water, in conjunction with the effects of fatigue and salt provisions That this particularly fatal epidemic was probably bacillary dysentery may be gauged from his frequent references to [illegible]

dysentery in the early p[illegible] Sir James Annesley's (1[illegible] and Treatment of the more [illegible] ction he gives a remarkably accurate pictorial and verbal illustration of [illegible] of the large intestine in both forms [illegible] liseases of [illegible] itiating in [illegible] ow known

[illegible] "Clinical [illegible] by James [illegible] *by Charles* [illegible] India," by Norman Chevers in 1886

[illegible] connected with the establish- [illegible] with the [illegible] nd living [illegible] was the first step; it was not until 1875 that a further great advance was registered. Then F. Lösch, in St. Petersburg, again found these organisms in a case of chronic dysentery, and by injection of the dysenteric material into the rectum of four dogs, found that dysenteric symptoms developed, with rectal ulceration in which amœbæ were proved to be present

[illegible] of this pioneer in Virchow's [illegible] themselves [illegible] satisfying [illegible] œbæ com- [illegible] the latter,

however, gained added authority through the investigations of Robert Koch in 1883 in Alexandria and in India; he again found these or-

afterwards confirmation came from the New World, in 1890, W. Osler, of Baltimore, demonstrated amœbæ in a case of dysentery with liver abscess originally contracted in Panama

Then, in 1893, W Kruse and A. Pasquale, again in Egypt, first put forward the novel suggestion of two species of amœbæ, one harmless and the other pathogenic, and they proceeded to prove their contention by producing dysenteric lesions by means of the intrarectal injection of cats with dysenteric stools and liver-abscess pus Another ten years then elapsed before the appearance of Schaudinn's historic paper wherein he traced the life-history of the human intestinal amœbæ, christening one *Entamœba coli* and the other, the pathogenic form, *Entamœba histolytica* In the meantime the differentiation of the epidemic from the more chronic form of dysentery was definitely established by the discovery and isolation of the dysentery bacillus by K Shiga in Japan in 1898

The history of the specific remedies employed in dysentery is almost as romantic as that of the causes of the disease

The use of ipecacuanha is a case in point This drug is the root of *Psychotria ipecacuanha*, a small plant from Brazil This is the official root and is known as Rio ipecacuanha; that from Colombia is distinguished as Cartagena ipecacuanha The first mention of "ipecaya" as a remedy for the "bloody flux" is made by a Portuguese friar and is published by Samuel Purchas in 1625 in "Purchas his Pilgrimes";* the use of this drug by the Indians is there discussed. After this time ipecacuanha or the "dysentery root" came into more common usage It is referred to in the work on the natural history of Brazil (1648) by Piso and Marcgraf, who described the plants to which the name was applied

Although the drug was in common use in Brazil, it does not appear to have been brought to Europe until 1672 It was prescribed by Helvetius, a Dutch physician practising in Paris, from whom the French Government bought the secret in 1688, paying £800 for it.

The use of ipecacuanha in dysentery was strenuously advocated by the great James Lind (1768), although it appears to have been introduced into general practice in the West Indies in 1726 by Richard

* For The Bloody Fluxe,

bedding in sea-water, in conjunction with the effects of fatigue and salt provisions. That this particularly fatal epidemic was probably bacillary dysentery may be gauged from his frequent references to strangury or *dysuria dysenterica* a frequent and disagreeable accompaniment of the infection. The first mention of dysenteric rheumatism in modern times is made by William Harty in 1805. To the horrors of the slave trade at this time must be added the effects, described by Thomas Winterbottom (1803), of dysentery amongst the human cargo; out of 700 slaves shipped at Sierra Leone, only some 380 lived to see Barbados. The first mention of drinking water as the infective agent in the West Indies is made by James M'Cabe in 1825.

Mention must also be made of the work of the great clinical physicians in India; thus James Johnson, who studied tropical diseases in his world-wide wanderings, published his experiences in "The Influence [illegible] on European Constitutions" in 1813, an account [illegible] Fellow of the [illegible] al Establish- [illegible] test work on dysentery in the early part of the nineteenth century is contained in Sir James Annesley's (1828) "Researches into the Cause, Nature and Treatment of the more Prevalent Diseases of India." In one section he gives a remarkably accurate pictorial and verbal illustration of liver abscess and the appearances of the large intestine in both forms of dysentery. To Sir George Ballingall, in a work on the diseases of European troops in India, must be given credit for differentiating in that country the two distinct clinical types of dysentery, now known as amœbic and bacillary.

Other works of this period which deserve brief notice are the "Clinical Illustrations of the More Important Diseases of Bengal," by James Twining in 1832; "Researches upon the Diseases of India," by Charles Morehead (1856); and a "Commentary on the Diseases of India," by Norman Chevers in 1886.

But no [illegible] connected with the establishment of [illegible] ascertain [illegible] amœbæ [illegible] first step; it was not until 1875 that a further great advance was registered. Then F. Lösch, in St. Petersburg, again found these organisms in a case of chronic dysentery, and by injection of the dysenteric material into the rectum of four dogs, found that dysenteric symptoms developed, with rectal ulceration in which amœbæ were proved to be present.

[illegible] in Virchow's [illegible] themselves [illegible] satisfying are the figures of D. D. Cunningham (1870), who found amœbæ commonly present in choleraic stools in India. The work of the latter,

CHAPTER IV

GEOGRAPHICAL DISTRIBUTION OF THE DYSENTERIES

Great Britain *England*—That bacillary dysentery exists in an endemic form and that sporadic cases of this disease occur from time to time, is now well established. Dysentery has played its part in English history Edward I died of relapsing dysentery in 1307 and Henry V of this disease in 1421 In recent years too, small epidemics of bacillary dysentery have been recorded It is probable that dysentery bacilli are normally present in a small proportion of the population, and the more general recognition of this disease is due to increasing knowledge and more careful investigation of patients suffering from diarrhœa.

A S. MacNalty reported two outbreaks of acute dysentery in London (Chelsea and Islington) during the autumn of 1917 It was considered that a close connexion with antecedent cases could be traced, and the prevalence of dysentery of the same type in the Army in France was held responsible for its introduction into London

G S Buchanan (1918) reported an outbreak of Shiga dysentery in an institution in the Eastern Counties, in which 38 cases were recorded with two deaths Flexner outbreaks have also been noted by A G M Severn and E N Evans in Smethwick, in August, 1927, and by J A Charles and S H Warren (1929) in Newcastle-upon-Tyne, between March, 1928 and June, 1929 The infection was mostly of the Flexner type and they conclude that it is a relatively common disease, this has been borne out by recent experiences

[illegible]

infection No cases of Shiga infection were found

Wales—A report made by T W Wade for the Ministry of Health describes an outbreak in the Ogmore Vale, Glamorganshire, in May, 1921, in which it is estimated that some 1,100 persons suffered from mild dysentery The outbreak followed a severe drought and was limited to a defined area, and evidence showed that houses situated near the source of the water supply were more seriously affected than those more remote Three hundred and twelve cases attended by

Towne, who gives minute instructions for its exhibition, which he modestly ascribes to the "learned and judicious Dr Friend."

James Sims (1773) in his "Observations on Epidemic Disorders," recommended two methods of exhibiting "ipecoanha" in dysentery, in so large a dose as to promote emesis, or, better still, in smaller doses with opium He was a pioneer in another respect also, in that he insisted on the value of this treatment in the *chronic* (or amœbic) form of the disease In Thomas Trotter's "Medicina Nautica" (1804) another method of ipecacuanha treatment was given, employing 12–15-gr doses daily Its chief merit was its emetic action in discharging the contents of the stomach

Subsequent to the writings of these pioneers, the use of ipecacuanha became more general and is frequently mentioned by the older generation of Indian physicians Patrick Manson shared to the full the belief of his predecessors in the sovereign value of ipecacuanha, and employed it exclusively in his practice from 1883 onwards. He recognized its efficacy not only in chronic dysentery, but also in liver abscess, and he evolved a technique of his own for its administration.

Almost as numerous as the speculations on the origin and nature of dysentery have been the variety of remedies suggested for its cure. Antimony oxide, in the form of James's powders* was recommended by Robert Jackson in 1817 and by numerous other writers. The use of opium has always been popular and a belief in its curative power has persisted almost to the present day. In 1796, C. Maclean used it in enormous doses in combination with calomel, and George Cleghorn (1751) was a firm advocate of opium for the ship dysentery of his day. Assalini (1801) dilates upon the "sovereign powers of opium" and the soothing effects of anodyne fomentations and tepid baths Thomas Clark (1801) advocates the exhibition of 3–5 gr. of James's powders* with an addition of a few drops of laudanum to promote perspiration.

The more modern treatment by the purgative action of saline aperients appears to have been adumbrated by Donald Monro (1780). In his opinion the important part of the cure depended on the use of gentle purges at the beginning of the illness to carry off the corrupted humours, the purgative being repeated every second, third and fourth day as the case required. Rhubarb was advised, although not so efficacious as saline purges.

John Rollo (1786) was a wholesale admirer of the laxative treatment, which he persisted in giving through the whole course of the disease. James McCabe (1825) was the first to employ charcoal extensively. Norman Chevers favoured the bael fruit in chronic dysentery, and also initiated the era of calomel in large doses (10 gr or more). Gradually from the tendency to employ cathartics, we see the development of the modern aperient treatment of bacillary dysentery

* JAMES'S POWDERS — Antimony oxide 33 per cent and precipitated calcium phosphate 67 per cent The dose is 3 gr *U S* National Formulary There is a history of James's powders by Michael Donovan in the *Pharm J.* 1869

In nine months of that year there were 810 cases of bacillary dysentery and only 13 cases of proven amœbiasis.

five times as common as amœbic

The appended tables are taken from the Report on the Health of the Army for the year 1935 (Vol 71) Further comment is unnecessary.

TABLE IV

NUMBERS OF CASES DIAGNOSED DYSENTERY, DIARRHŒA, AND COLITIS DURING PERIODS 1920-1925 AND 1930-1935

	British Other Ranks				Indian Other Ranks			
	1920-1925		1930-1935		1920-1925		1930-1935	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Bacillary dysentery	402	16	5,470	3	241	9	7,892	17
Amœbic dysentery	3,176	25	1,079	0	3,272	47	814	1
Clinical dysentery	497	7	1,987	1	4 281	74	2,767	11
Diarrhœa	5,878	0	4,960	0	14,627	8	6,065	0
Colitis	1,420	3	187	0	15,485	42	167	2
Total	11,373	44	13,693	4	37,906	180	16,705	31

The extraordinary contrast in the diagnoses, the large reduction in the number of deaths and the slight increase in admissions among British troops, as compared with the huge fall in total admissions among Indian troops, can perhaps be better appreciated if only the difference in admissions between the two periods are observed, as in Table V

TABLE V

TOTAL ADMISSIONS FOR DYSENTERY, DIARRHŒA AND COLITIS DURING 1930-1935 CONTRASTED WITH THOSE DURING 1920-1925

	Bacillary dysentery	Amœbic dysentery	Clinical dysentery	Diarrhœa	Colitis	Total admissions for group	Deaths
British troops	+ 5 068	− 2 097	+ 1 490	− 918	− 1,233	+ 2 310	− 40
Indian troops	+ 7,651	− 2,458	− 1 514	− 9,562	−15,318	−21,201	− 149
Total	+ 12,719	− 4,555	− 24	−10,480	−16,551	−18,891	− 189

The distribution of Sonne dysentery is dealt with in the section devoted to that subject (p 68).

local practitioners were distributed in 148 houses, and no less than 32 9 per cent of the occupants of these houses were attacked. There were 12 deaths during the height of the epidemic—five in infants under one year of age The outbreak was due to a Flexner bacillus of the W type

Ireland.—In August, 1919, A Stokes and J. W. Bigger described an epidemic of bacillary dysentery in Dublin, the first recorded in modern

of 189

dysente

cent

the organisms

India.—So many references will be made to dysentery in India in subsequent pages, and so much of first-rate importance has been written upon the ætiology of the disease in that country, that an elaborate account cannot be undertaken here As to the true relationship of one form of dysentery to the other, it is very difficult indeed to form a just estimate, since the methods of diagnosis and the statistics set forth have varied so much from time to time.

In the summaries recorded in the League of Nations Report for 1930 *for the whole of India, a bacillary diagnosis was made in 64 6* per cent, among both British and Indian troops. The proportion of amœbic dysentery was given as 8 4 per cent. among the Indian troops and 15 6 per cent among the British.

cent. (responsible for most of the deaths); and Sonne, 2 2 per cent.

The experiences of J. A. Manifold (1926) on important features in

where previously the main form of the disease had been thought to be amœbic. The figures they published have entirely reversed the proportion which the two main forms of dysentery held to one another.

Protozoal or Endemic Dysenteries.

(a) AMŒBIASIS, or infection with the dysentery amœba (*Entamœba histolytica* (Schaudinn)

This term includes.—

1 Primary intestinal amœbiasis or "amœbic dysentery"

2 Secondary amœbiasis (complications of 1)—hepatic amœbiasis, amœbic liver abscess, etc.

(b) BALANTIDIASIS, or infection of the intestinal canal with an infusorian, *Balantidium coli* This is a rare infection, but is quite commonly found in lower animals

(c) COCCIDIOSIS infection with *Isospora hominis*, a rare infection of the intestinal tract of man about which little is known

(d) GIARDIASIS, or lambliasis, an infection of the small intestine with *Giardia intestinalis*, a protozoan flagellate

(e) FLAGELLATE DIARRHŒA, or infection of the intestinal canal with protozoan flagellates—*Trichomonas hominis* and *Chilomastix mesnili* This is a rather doubtful pathological entity

(f) MALARIAL DYSENTERY, occurring in the course of infection with *Plasmodium falciparum*

(g) LEISHMANIAL DYSENTERY, occurring in the course of kala azar (*Leishmania donovani*), usually a terminal event

Metazoal or helminthic dysenteries—A dysenteric syndrome brought about by ulceration or inflammation of the intestinal tract by helminths, of which *Bilharzia* is the most important The eggs of these parasites, in passing the intestinal walls, give rise to ulceration and papilloma-formation which in turn cause dysenteric symptoms Other species of helminths also may give rise to similar symptoms

CHAPTER V

DYSENTERY : CLASSIFICATION

It is always a matter of difficulty to define exactly what is meant by the term "dysentery," mainly because many phases of the diseases included under this heading are not characterized by dysenteric symptoms as generally understood The term "Dysentery" is derived from the Greek δυσ-εντερία or δυσ-εντέριον (a bowel complaint) and this definition if properly appreciated, explains the main outstanding symptoms To the popular mind it indicates passage per rectum of blood-stained mucus derived from the bowel wall The passage of these abnormal intestinal contents is attended by generalized abdominal pain or discomfort, and is usually accompanied by tenesmus or straining

The term dysentery has become applied to a symptom-complex which, as modern research has revealed, may be produced through the infection of the bowel itself, or the invasion of its walls, by many different organisms Thus it can readily be realized that diagnosis of the dysenteries and, consequently, their treatment, may become a very recondite and intricate problem It must be remembered that diseases essentially of wide and distinct ætiology may resemble each other closely in outward appearances, and hence it becomes necessary to correlate, as has been attempted in these pages, the clinical, pathological, bacteriological, and protozoological aspects before an expert opinion can be given on any individual case

It is customary and indeed convenient, to classify the dysenteries by dividing them into main headings according to whether they are of bacterial, protozoal, or metazoal origin The following classification has therefore been evolved —

Bacillary or Epidemic Dysenteries, caused by the dysentery bacilli.—

- (i) Shiga's bacillus (*B dysenteriæ Shiga* Syn. *Eberthella dysenteriæ*)
- (ii) Schmitz's bacillus (*B dysenteriæ Schmitz*)
- (iii) Flexner's bacillus (*B dysenteriæ Flexner* Syn. *Eberth paradysenterica*)
- (iv) Sonne's bacillus (*B dysenteriæ Sonne*,* probably identical with *B dispar* (Andrewes).

* Also known as the Kruse-Sonne bacillus

The Bacillary Dysenteries

The Bacillary Dysenteries

CHAPTER VI

THE BACILLARY DYSENTERIES

Synonyms.—Acute or epidemic dysentery

French Dysenterie bacillaire
Italian Dissenteria bacterica
German · Bazillenruhr
Japanese Ekiri

Definition—A group of infectious diseases caused by invasion of the colon, and occasionally also of the ileum, by bacteria of dysentery

Usually pyrexia, griping, and tenesmus are present in varying degree An outstanding clinical feature is intoxication due to absorption o dysenteric toxins This condition may become chronic and lead to chronic bacillary dysentery The most frequent complication is inflammation of the synovial membranes

ÆTIOLOGY

Predisposing causes include unsuitable food, exposure to extreme heat or cold, errors of drink and diet, and fatigue, especially during

age of five are specially liable to bacillary dysentery, as are also those whose resistance has been lowered by any chronic and debilitating

ntery

on or

from cooking utensils and food and can only occur where the habits of the people are insanitary, it is undoubtedly a factor amongst primitive natives In lunatic asylums direct contagion plays a prominent part, and it has been pointed out that in these institutions the main focus of infection is the latrine

It is probable that cases of endemic bacillary dysentery which were

noted in England during the 1914-18 War were due to direct infection contracted from returned soldiers who were convalescing from this disease Such an instance was recorded by P. L. Sutherland in Wakefield, Yorkshire, in 1916

2 Indirect contagion. Dysentery bacilli can be conveyed by the

conveying the infection by transferring it to foodstuffs. In the Pacific Islands house-flies constitute a great plague in the dysentery season, and they are attracted by fæcal material, especially dysenteric stools, on which they feed readily The bacillus can be conveyed to food by the fly in two ways. firstly, by vomiting ingested dysenteric material directly on to the food—its normal prelude to feeding—and secondly, by defæcating on to any article of diet in the kitchen or on the table.

It has generally been noted that epidemics of house-flies coincide very closely with those of bacillary dysentery, and that the incidence of the disease diminishes during the season when these insects are comparatively rare This takes place, in the Middle East and in Africa, during the hot season when the majority of the larvæ are destroyed by the rays of the sun. As originally pointed out by the author in 1912, it is possible by appropriate technique to isolate the dysentery bacillus, especially *Bact shigæ*, from the intestinal contents of house-flies caught in association with dysentery patients, and to demonstrate their presence in the intestinal tract of the insect for five days after ingestion.

S T Orton (1910) investigated an outbreak of 186 cases of dysentery in the Worcester State Hospital, U S.A, and concluded that flies, which were present in great numbers, were responsible A. Krontowski in 1913 fc

dysentery

three days

isolating S

dysentery patients.

In 1919 the author repeated his original experiments with wild

should be repeated.

It has repeatedly been pointed out by other observers that there was some intimate association between house-flies and dysentery, for instance, by W E Musgrave and A G Sison in 1914 in the Philippines; and by J Morison and W. D Keyworth (1916) in their study of flies in relation to epidemic diarrhœa and dysentery in Poona. J. Koch (1916) came to the same conclusion in his study of war dysentery in Germany, and N. Paichme in his study of fly-borne disease in South Africa H Otto, in the war epidemic in Poland in 1939 definitely associated bacillary dysentery with flies, aided by direct contact amongst troops and hospital nurses Reports from the Forces in the Middle East (1941) have amply confirmed these observations

General observations on the house-fly—Micro-organisms are conveyed either externally or internally by the fly from the source of infection Some organisms, mainly bacteria, survive drying only for a few hours, while others, spore-producing varieties, can survive for prolonged periods As a means of transferring bacteria the body of the fly is most excellently adapted, clothed as it is with hairs or setæ of varying lengths. Its legs, which are brought frequently into contact with infected material, closely resemble miniature brushes to which the organisms tenaciously adhere, as a result the fly contaminates whatever substance it may subsequently visit within a certain time

Most observers have concluded from their experiments that the possibility of flies becoming infected through the presence of pathogenic organisms in the breeding-ground of the larvæ may be considered remote

[illegible]

infecting themselves with bacilli derived from mild unrecognized cases and "carriers" and the same is probably true for dysentery bacilli

Water and the spread of bacillary dysentery—There appear to be adequate reasons for incriminating water as a factor in the spread of bacillary dysentery. In experiments made by the author in Fiji (1912) bacilli could be recovered after four weeks from sterilized water impregnated with Shiga's bacillus and after six weeks from tap-water

L [illegible]
be [illegible]
hou [illegible]
in [illegible]
was found that, when so kept, the bacillus retained its cultural and agglutinative characters Apparently chlorination of water does not render it absolutely safe from infection, for Dudgeon found that when chlorinated under expert guidance it was still capable of being infected with the Shiga bacillus Dysentery bacilli are readily destroyed by direct action of the sun's rays and probably cannot survive long in

water which has been so heated. Despite this evidence, the author was unable to convince himself that, under modern war conditions, water played any great part in the dissemination of dysentery.

The spread of bacillary dysentery by milk.—Various outbreaks of bacillary dysentery (Flexner) have been ascribed, more or less on insufficient evidence, to contaminated milk; but in Sonne dysentery this appears to have been definitely proved (G. K. Bowes, 1938).

Causal organisms. *History*.—K Shiga (1898), at Kitasato's suggestion, identified the ætiological agent of acute dysentery by applying agglutination tests to bacteria he isolated from dysentery stools. This organism he obtained from 34 out of 36 cases, and he subsequently inoculated himself subcutaneously with a killed culture of the bacillus, with the production of a severe local reaction. His original account was supplemented and augmented by others in 1901, 1902 and 1908. Two years later, an almost identical discovery was made by W. Kruse (1900), of Bonn, who found the same bacillus in dysentery cases in Laar, Westphalia, while S. Flexner, also in 1900, found in dysentery in the Philippine Islands a bacillus he thought at first was the same as that of Shiga About the same time R P. Strong and W E Musgrave found similar organisms in Manila It remained for E Martini and O Lentz (1902) to demonstrate that the bacilli of Shiga and Kruse differed from those of Flexner and Strong in their serological as well

in isolating from cases of fatal diarrhœa in children an organism they called the Y bacillus, which ferments mannite as well as dextrose. Since that time

Modern bacteriologists recognize .—

(1) The non-mannite fermenters, of which the most important are Shiga's bacillus—*Bacterium shigæ*—and Schmitz's bacillus—*Bacterium schmitzi*. In 1917 K G F Schmitz described a bacillus closely resembling Shiga's bacillus, but differing in production of indol from peptone and producing a distinct antigen.

known as varieties of

strains (formerly known

bacillus etc.); for details

see p

(3) The late-lactose fermenting group represented by Sonne's bacillus—*Bacterium sonnei*, which produces a distinctive clinical syndrome and which is becoming increasingly important

Other bacilli have been described and accredited a rôle from time to time in the production of dysentery Morgan's Bacillus No 1, resembling *Bact. coli*, has recently been discredited; so also has *Pseudomonas pyocyanea*

(*B. pyocyaneus*), which is widely distributed in water, sewage, etc., and which may appear in numbers in the stools and on culture may inhibit the growth of the true dysentery bacilli

Dysentery bacteriophage.—During the last twenty years d'Herelle has devoted considerable attention to the elaboration by dysentery cultures of a special bacteriophage This dysentery-phage is specific for both Shiga and Flexner groups, and is apparently produced in the intestinal canal of patients recovering from bacillary dysentery Great hopes were entertained that this discovery would result in a potent remedy and prophylactic, but unfortunately these have not been realized The whole subject of dysentery-phage is discussed in d'Herelle's work "The Bacteriophage and its Behaviour" (1926)

The nature of
consists of ult
(millimicron)
limits of its filt
d'Herelle to be a protobacterium, either derived from the bacterium itself as an enzyme, or a living autonomous thing which uses bacterial substances in

members of that group

Bacteriophage is isolated from the stools of patients convalescent from

appears that improvement in the patient's condition coincides with the moment when virulence of the bacteriophage excreted in the stools dominates resistance of the dysentery bacteria Thus there are reproduced in the living body the same phenomena as in the test tube

D'Herelle has found in fatal cases of bacillary dysentery that at no time during the course of infection does the intestinal bacteriophage show any activity for Shiga's bacillus, either for the stock strain or for those isolated from the stools of patients From this it is argued that in an epidemic

... cases of aborted bacillary dysentery.

bacteriophage

With a view to establishing a specific therapy, d'Herelle himself ingested increasing quantities (from 1 to 30 c c) of bacteriophage suspensions aged

and so on

D'Herelle has quoted a series of cases of bacillary dysentery treated by the administration of specific bacteriophage, this form of therapy being limited at first to cases in which the infection was proved by isolation of the pathogenic organism

virulence

Bacillary dysentery in animals.—Bacillary dysentery has rarely

Reproduction of dysentery in laboratory animals.—Shiga's *bacillus is especially toxic for rabbits, horses and mice, but to a much* lesser extent for guinea-pigs Sometimes after subcutaneous inoculation, especially in rabbits, the
give rise to intense cat
(Vaillard and Dopter, 19
differ considerably from
young pigs the infection becomes generalized, and the organisms can be recovered from all the viscera Possibly a fatal issue takes place too rapidly for dysenteric lesions of the bowel, as seen in human subjects, to develop fully In laboratory animals subcutaneous inoculations produce intense inflammation at the site of injection, accompanied by pyrexia This is sometimes followed by paresis of the hind quarters and occasionally also by severe diarrhœa with blood and mucus

Reproduction of the disease in man.—In 1900, R. P Strong and W. E. Musgrave reproduced bacillary dysentery in a condemned criminal by administering by the mouth a 48-hour culture of Flexner's bacillus The man recovered after a typical attack of bacillary dysentery, and the organism was recovered from his stools

There are three authentic cases of accidental laboratory infection of bacillary dysentery in man W Kruse (1901) mentions a doctor in his laboratory at Bonn who infected himself with cultures of Shiga's bacillus, and thereafter suffered from a mild attack S Flexner (1900), in Baltimore, described the case of one of his assistants who accidentally aspirated a culture by the

[illegible]

clinical dysentery developed and the same bacillus was isolated from the stools

Carriers of bacillary dysentery.—These may be classified as healthy, convalescent, relapsing, and chronic carriers

[illegible]

group is not important for, since the cases reported by Kruse, Conradi

[illegible]

excreting Flexner's bacillus K Saisawa and B Tanabe (1926) examined 2 [illegible]
cent. wer [illegible]
examined [illegible]
83 carrie[illegible]
and the "Y" bacillus in 17

The majority of bacillary-dysentery carriers are *convalescent carriers*, i e, persons who, after an attack of bacillary dysentery, continue to pass viable bacilli in the fæces, usually together with blood and mucus Saquépée considers that the *formes frustes*, the slight and clinically almost unrecognizable forms of the disease, play an important part in its spread

Friedmann in 1913 reported an epidemic in which eighty-six men in a cavalry regiment were attacked, and which was eventually traced to a convalescent carrier, and in 1921 Keersmakers described an extensive epidemic amongst the Brussels garrison which was traced to a prisoner of war who had recently returned from Germany

J A. Arkwright, W Yorke, O H Priestley and W Gilmore found that two out of fifty convalescent dysentery patients were excreting Shiga's bacillus six months after the attack A M Kennedy and D D Rosewarne found only six carriers, of which three were Shiga and Flexner [illegible]

[illegible]

in the intestinal canal N. P. Hudson has reported upon such a case. The patient contracted Flexner dysentery in June, 1918, and during a relapse three and a half years later, in January, 1922, the bacillus was again isolated. The author has had a similar experience: an officer contracted Shiga dysentery in April, 1917, the bacillus being isolated on culture; exactly three years later he suffered from a clinical relapse in England, during which the same organism was isolated

The *chronic carrier* may be defined as one who is incompletely cured of the disease in a clinical sense, and continues to pass dysentery bacilli in the fæces The importance of this factor was amply confirmed in the 1941 Libyan campaign

W Fletcher (1917), working in England on War convalescents, found only one carrier of Shiga's bacillus among 800 men: on the other hand, dysentery bacilli of the Flexner type were isolated in 2 25 per cent. Again W. Fletcher and D L Mackinnon in 1918 found that Shiga carriers were rare in a group of 935 war convalescents—1.39 per cent.—while 61 were Flexner carriers E Sergent and L. Nègre found 13 chronic carriers among a group of 67 pilgrims who had recently returned from Mecca

[illegible] According [illegible] intestinal [illegible]

(a) Retention cysts in the submucosa, originally described by the author (Fig. 8)

(b) Collections of pus which form beneath the pigmented scars of healed ulcers.

(c) Undermined margins of chronic ulcers

The carrier state in bacillary dysentery does not, as a rule, persist for any g [illegible] to this p [illegible] usually I [illegible] only 4 per cent were still carrying dysentery, in the case of Flexner infections it was higher, 7 per cent. T [illegible] last at most [illegible] of Flexner [illegible] three and a half years

The great majority of carriers, even when apparently healthy, are still suffering from ulceration of the intestinal mucosa; wherever sigmoidoscopy has been carefully performed, as in the series investi- [illegible]

has proved of little avail (W Fletcher, 1917) Recently sulphaguanidine treatment has proved valuable.

The detection of carrier cases corresponds with the annual seasonal outbreaks of bacillary dysentery in the Philippines, and appears to run parallel with the number of clinical cases

Dysenteric toxins.—In 1903 H Conradi produced an autolysate of Shiga's bacillus which was toxic for rabbits and guinea-pigs After incubation, an 18-hours-old culture was suspended in saline and further incubated for 24–48 hours at 37° C , when centrifuged, the yellowish supernatant fluid was diluted with five times its volume of saline and filtered through a Berkefeld candle This product, injected sub-

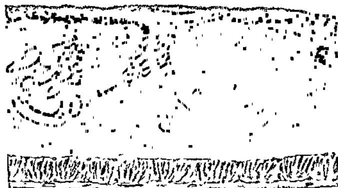


Fig. 8 —Chronic bacillary dysentery (Shiga infection) : microscopic section showing formation of submucous retention cysts from adenomatous extensions of Lieberkuhn follicles.

cutaneously into guinea-pigs in a dose of 0 1 c c , proved fatal in 48 hours, in rabbits death was preceded by diarrhœa, collapse, and paralysis of the extremities Neisser and Shiga further noted that these toxic substances were precipitated by alcohol and ether and destroyed by heat at 75° C while C. Todd (1904) prepared a soluble toxin which was highly active in rabbits and horses, but much less so in guinea-pigs, rats, and mice Dopter (1905) described definite lesions in the spinal cord, chiefly chromatolysis of the anterior horn cells, and these were noted as frequently after injection of toxin as after

concluded that there are two toxins, one, paretic or neurotoxin, causing

paralysis of the muscles, the other, intestinal toxin, causing diarrhœa and chronic marasmus

The dysenteric toxins are very resistant to heat and to the action of light and ferments; their activity is neutralized when they are emulsified with fresh mucous membrane, especially that of the rabbit's intestines

W W C. T[illegible]
knowledge of
soluble toxin
bacillus are much more potent than those of the Flexner group, some strains of the latter having actually been proved to be completely a-toxic

As regards the nature of the toxin, it is believed to be intermediate in position between an exo- and an endotoxin, possessing some of the properties of each In order to prove that the dysentery endotoxin is distinct from the exotoxin, it would be necessary to show that an anti-exotoxic serum has no neutralizing effect upon the endotoxin, but it has been found that such a serum will neutralize Shiga toxin whichever way it is prepared

K Schroer (1940) has studied the toxins of Schmitz's bacillus The exotoxin was obtained from a filtrate of broth cultures by precipitation with trichloracetic acid, and the endotoxin from young cultures grown on agar The endotoxin is rather weaker than that of Shiga's bacillus Rabbits are most sensitive to exotoxin, guinea-pigs to endotoxin The conclusion is reached that, in production of toxins, Schmitz's bacillus occupies a position between active *B. shigæ* and inactive *B flexneri*

C. C Okell and A V Blake (1930) produced a modified toxin-toxoid This is prepared from the filtrate toxin by the addition of 0 6 per cent formaldehyde, so that after three weeks at 37° C. the original toxin becomes innocuous A horse immunized with toxoid, however, yielded a very potent antidysentery serum after six weeks' treatment.

Habitat of the dysentery bacillus in the human body.—The dysentery bacillus is an inhabitant of the intestinal canal and, in the great majority of cases, solely of that tract. It is found mostly in the mucous membrane of the lower part of the small, and through the whole extent of the large intestine The organisms

comparative ease from the inflamed mucous membrane, and occasionally at autopsy from inflamed mesenteric glands

Dysentery bacilli have rarely been found in the blood, gall-

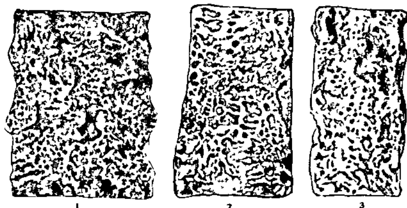


Photo Dr G. Mather Cordiner

Barium enema of chronic bacillary dysentery (Flexner infection), showing smooth outline of bowel, patches in descending colon, and normal outline of the cæcum

CHRONIC BACILLARY DYSENTERY

PLATE I



1, Acute bacillary dysentery necrosis 2, Diphtheroid membrane in bacillary dysentery. 3, Subacute bacillary dysentery.



4, Chronic bacillary dysentery. 5, Mixed infection of amœbic and bacillary dysentery; *A—amœbic ulcers, B—bacillary necrosis of mucosa.*

PATHOLOGY OF THE COLON IN BACILLARY DYSENTERY

(Drawn by P H Manson Bahr, after W Fletcher and M. W Jepps

PLATE II

bladder, urine, and spleen. L. Rosenthal (1903) isolated Shiga's bacillus [illegible]

morter [illegible]
bacillı [illegible]
Ledin [illegible]
bacillu [illegible]
typhoi [illegible]

bacillus from the blood and spleen in Germany, and L Dudgeon in 1919, in Salonica, succeeded in obtaining it from the blood twice out of 145 attempts. P. C. Flu (1918) [illegible]

[illegible] with cerebral symptoms, the bacillus being also isolated post mortem H Spranger (1926), in Germany, by using a special bile medium, succeeded in isolating Shiga's bacillus twice, Flexner's bacillus once, and the Y bacillus once, by blood culture

The dysentery bacillus has, very occasionally, been grown from the bile at post-mortem, for example by A. Ghon and B Roman (1915) in Germany, and by A Connal and E C. Smith (1925) in Nigeria P C Flu in 1918 found that bile does not definitely inhibit growth of dysentery bacilli, and he was able to isolate the organism from it two months after the last intravenous injection of Flexner bacilli into rabbits C W. Duval and Bassett (1903) recorded isolation of Shiga's bacillus from the liver

Records of isolation of the dysentery bacillus from urine are scanty S. R Bruenauer (1916) obtained dysentery bacilli in four out of fifty-four bacteriologically proven cases A. Ghon and B Roman [illegible] nd [illegible] ry. [illegible] he [illegible] lus [illegible] from the synovial fluid in dysenteric arthritis He employed a large amount of joint exudate for the purpose, and as a result four colonies [illegible]

[illegible] epidemic form in highly cultured northern European countries Dysentery was rife in mediæval England at a time when filth, squalor and

overcrowding were only comparable with primitive tropical conditions at the present day In recent years epidemics have been recorded in France, Germany, Great Britain, and the United States. In civilized countries the disease especially affects small children, in whom it may cause a considerable mortality. In these countries too, it is endemic in

Prussian Guard at Döberitz in 1901 (Drigalski) In Russia, under the Soviet régime widespread and extensive epidemics have been recorded. That bacillary dysentery is by no means necessarily associated with high atmospheric temperatures is shown by the fact that outbreaks resembling this disase have been recorded in sub-arctic countries.*

Bacillary dysentery has always been associated with the armies in the field It apparently decimated the armies of Napoleon on the retreat from Moscow, it was present in the Crimean War; it was the chief form of dysentery in the South African War of 1900-02 (38,108 cases with 1,342 deaths), and it was undoubtedly a feature of the Franco-Prussian War of 1871, leading to epidemics in Germany which lasted for several years In the 1914-18 War it furnished a considerable proportion of the casualties on all fronts, especially in Gallipoli, Salonica,

nce

In

in

France, and no less than 486 per thousand in East Africa, while in Gallipoli, in August, 1915, it was responsible for a high proportion of the 120,000 medical casualties evacuated from the Peninsula within three months.† To quote Shiga, "it is always a constant companion of war, and it has been more fatal to armies than powder or shot."

In India, Malaya, and the Pacific Islands, bacillary dysentery is responsible for widespread and particularly fatal epidemics. In the Fiji Islands, for instance, epidemics in 1884 caused a mortality rate of over 130 per thousand, and even in recent years it has varied from 52 to 128 per thousand

Wherever it occurs, bacillary dysentery is likely to appear in epidemic form, and these epidemics are usually subject to seasonal variations; in the tropics, where there is a well-marked wet season, the disease tends to appear at the end of the rains In India, also, where bacillary dysentery epidemics are of annual occurrence, L. Rogers (1913) has shown that a characteristic seasonal incidence occurs. During the colder months of January and February bacillary dysentery almost disappears, to rise with the advent of the warmer weather; but in

the very hot May and June there is a fall The maximum increase follows closely on the monsoon rains in July, reaching its peak in August and September

Balfour Kirk has summarized the epidemiology of bacillary dysentery in the tropics as follows :-

(a) Rains deter occupants from defæcating at a safe distance from their villages

(b) Waterlogging of the soil prevents bacilli from dying out

(c) The people are more liable to chills which precipitate an acute or subacute attack

commonest was a subvariety of the latter named El Tor No 1, from which these workers prepared a therapeutic antiserum

Bacillary Dysentery in its Relation to Intestinal Amœbiasis

It is probable that no proper conception can be obtained of the true distribution of bacillary dysentery from isolated published statistics or from official sources There are two main factors to account for discrepancies which will be found in this particular section :—

1 The bacillary disease can only be diagnosed with scientific certitude by isolation of the dysentery bacillus, and this is a procedure demanding skill, a properly equipped laboratory, an experienced scientific director, and the provision of adequately trained laboratory assistants Such facilities are not to be found everywhere in British Crown Colonies and in the more undeveloped portions of Central Africa and Central America

2. The recognition of amœbic dysentery and the differentiation of *Entamœba histolytica* from the non-pathogenic amœbæ require the attention of a properly trained protozoologist The number of specially trained personnel is limited, and many are the pitfalls which beset the tyro in the identification of the true dysentery amœba in all its

popular attention than in northern climes

There is at present no uniformity in the matter of diagnosis nor general agreement on the basis by which these diagnoses are made, and until there is some universal and generally accepted standard, discrepancies and paradoxical statements are bound to be noted and

sudden *bouleversements* of statistics to occur from time to time. We

phases, are much more intricate and difficult to detect than are protozoal

For more detailed information regarding the world incidence of the two main forms of dysentery, the reader is referred to Table X, pp. 136–150

CHAPTER VII

THE BACILLARY DYSENTERIES (*continued*): PATHOLOGY, SYMPTOMATOLOGY AND COMPLICATIONS

Mild cases.—It is difficult to describe the pathological appearances of mild bacillary dysentery because since patients do not succumb to mild infections opportunities for post-mortem examination are infrequent The earliest lesions noticed by the author appear to origin-

secretion of viscid mucus

Very acute cases.—The fully developed pathological picture appears to consist of acute hyperæmia of the large intestine which

virulent cases death may take place in as short a time as fifty-six hours from the onset

Stage of hyperæmia—At autopsy the appearance of the cadaver suggests intense toxæmia, but there is no wasting. There is paralytic distension of the large intestine, the mucosa is found to be bright scarlet red, very friable, dripping with blood, but there is no infiltration of the walls of the viscus The lumen of the bowels is filled with viscid mucus intermingled with blood, in the small intestine there is a similar outpouring, tinged green with bile Abundant signs of wide-spread toxic absorption are usually found. Thus, a general lymphoid peritonitis is present, with exudation of free serous fluid into the peritoneal cavity, lymphoid flocculi of the peritoneal surface, and œdema of the mesentery The mesenteric glands are enlarged, red,

and softened Very commonly post-mortem intussusception of the small intestine is present There is engorgement of the right side of the heart, the liver and kidneys, enlarged and congested, show parenchymatous degeneration (toxæmic nephrosis); the gall-bladder contains scanty, tenacious, amber-coloured bile; the spleen is dark red and slightly diffluent the suprarenal glands may show central necrosis.

In less acute cases which do not run such a rapid course, the mucous membrane has a rosy plum colour, mottled with numerous submucous hæmorrhages while the whole bowel is œdematous and consequently much thicker than normal (Plate IV, 1, facing p. 66) The numerous extravasations of blood into the submucosa constitute the acute hæmorrhagic type H R Dew and N H. Fairley (1921), describing the pathology of a series of 259 acute and fatal cases, noted, together with the acute changes in the intestines, toxic spoiling of the viscera In one instance Flexner's bacillus was obtained from a splenic abscess Myocarditis and pericarditis were common

Stage of necrosis —In those who survive this process for more than a week, the stage of coagulation-necrosis is reached. Then the cadaver shows very considerable signs of wasting. The large intestine, especially the sigmoid flexure, is spastic and narrowed. The bowel wall is thickened by œdema, hæmorrhages, and cellular infiltration The appendices epiploicæ are engorged, discoloured, even œdematous. *The defunct mucous membrane is converted into an olive green,* [illegible]

[illegible]

intestinal contents consist of dark greyish fluid containing altered blood but, owing to destruction of mucous cells, show little mucus The necrotic mucous membrane can be scraped off with difficulty, revealing [illegible] ...osis are [illegible] inter- [illegible] ...ists in [illegible] ...ulating [illegible] ...ossibly recover, and even if this were possible, occlusion of the lumen would result. In this type of dysentery death usually takes place at the end of the third week By this time the body is emaciated, the subcutaneous fat has completely disappeared; the omentum is denuded of its fat; the abdominal viscera are wasted, and the mesenteric glands hard and fibrous Where the necrotic process affects only limited portions of the bowel, ulcers of an irregular outline tend to form Usually they are oval or irregular and communicate with each

other by submucous burrows or sinuses This riddled appearance involves the whole of the large bowel (Plate II, 1–4)

P. Remlinger and J Dumas (1915) describe an acute suprarenal syndrome in 4 per cent. of bacillary dysentery cases The diagnosis is verified at autopsy by finding the adrenal hypertrophied The

clinical state to Simmond's disease has been noted

The stage of recovery—When the mucous membrane has been as completely destroyed as in the description already given, it is difficult to visualize how it can be restored to its normal condition Observations indicate that regeneration of the mucous membrane takes place from islands of mucosa which have escaped destruction Repair appears to consist of proliferation of the columnar epithelium and the laying down of fibrous tissue, the healing mucosa being represented by a

Where this has failed,
lation tissue extending
itestine or in scattered
patches, especially in the lower portion Over-production of granulomata may result in pseudo-polyposis The transverse colon is sometimes distended and sacculated Often coils of the large and small intestine may become matted together by plastic peritonitis Pericolonic thickening and general hyperplasia of the large bowel, as observed in chronic amœbiasis, do not follow

The more advanced chronic lesions have been observed in pensioners from the 1914-18 War, and are common enough in natives, who suffer frequently from recurring attacks of longstanding bacillary dysentery These lesions consist of irregular ulcerations of the mucosa which rarely penetrate beneath the muscularis layer In a certain proportion of Europeans who have contracted chronic dysentery the main lesions appear as a granulomatous mucous membrane without demonstrable ulceration. In bacillary dysentery the ulcers are irregular in shape and run at right angles to the long axis of the bowel, the edges are not undermined and the base consists of greyish or brownish slough. In the chronic form pseudo-polypoid granulomata are sometimes so extensive as to occlude the lumen Further features are given in the accompanying comparison

Chronic Bacillary Ulceration	*Amœbic Ulceration*
Ulcers commence on free edge of transverse folds, and run at right angles to the long axis of the gut. Ulcers are serpiginous with ragged edges; they often communicate *with neighbouring ulcers and, as a* rule, involve the muscularis mucosa.	Ulcers commence as small abscesses in the submucosa which, on rupturing, ulcerate and are distributed parallel to *the long axis of* the gut. Ulcers are oval, regular *with undermined edges, rounded or* heaped up margins; discrete, flask shaped on section, involving mucous membrane, submucosa and muscular coats. They originate in the submucosa.

Perforation of the bowel as a result of bacillary dysentery may take place, although it is very rare compared with chronic amœbiasis. The author recorded (1919), in a series of over 300 autopsies in Egypt, three instances of ante-mortem perforation of the transverse colon with general peritonitis.

Retention cysts.—The author described a curious pathological condition which is the direct sequel of chronic bacillary dysentery and which *is frequently seen in autopsies on Eastern natives—the formation* of tapioca-like, mucous retention cysts, varying in size from that of a *hemp seed to that of a cherry, which are distributed unequally through* the large intestines, causing excrescences on the peritoneal surface; *on incision, clear, jelly-like mucus can be expressed. The retained* material is often infected with Flexner bacilli and with *B. coli*, and *may ultimately result in abscesses within the bowel wall. These cysts* form from proliferation of the mucous membrane beneath the muscularis and explain the intractable *mucous colitis* which is so *frequently* a sequel and which is so difficult to treat. W. Fletcher and M. W. Jepps (1924), *in their studies on dysentery in the Federated Malay States*, describe this condition as quite common in chronic cases and in carriers. *Repair of chronic ulceration takes place extremely slowly by the formation* of pigmented scars which are visible as bluish depressions, beneath which lie retention cysts. *(Fig. 8, p. 41.)*

Mixed infections.—The *frequency* with which *tuberculous* ulcerations and hyperplastic *tuberculosis* of the large intestine are noted *in natives of the tropics* who have *suffered previously from* bacillary dysentery makes it probable that the damaged mucous membrane offers lowered *resistance to tubercular infection.*

Amœbic ulceration may co-exist with bacillary disease. Typical lesions *are superimposed on a fibrotic and scarred bacillary bowel*; and, *per contra*, the author has seen acute bacillary dysentery grafted on *amœbic ulceration*, *but these cases are by no means frequent.* (Plate II, 5.)

Chronic bacillary dysentery *may*, also, be the starting-point of a fatal generalized *B. coli* pyæmia; and the author, in association with





P H Manson Bahr del

1 2

1 Amœbic Dysentery — Typical patches of infiltration and ulcera [illegible]

destroyed mucous membrane.

INTESTINAL LESIONS IN AMŒBIC AND BACILLARY DYSENTERY (Half nat size)

PLATE III

commonly encountered in tropical practice

B coli infections —J I Enright and the author in 1917, in Cairo, described amongst Turkish and Arab prisoners of war a pyæmia in which the kidneys were specially affected, caused by *B coli communis* or allied organisms

dysentery, and parenchymatous degeneration of heart, liver, spleen and kidneys was evident In smears from the organs the colon bacilli showed marked polar staining The bacilli isolated in pure culture from abscesses in the cortex of the kidneys were divided into nine groups by their sugar reactions Three failed to ferment lactose, and a type corresponding to *B neapolitanus Emmerich* was most frequently encountered

Protozoa and their cysts in bacillary-dysentery exudates —The existence of mixed infections of amœbic and bacillary dysentery may cause confusion to pathologists and clinicians That such infections do exist there can be no reasonable doubt On two occasions the author found active *Entamœba histolytica* in a stool with a characteristic bacillary-dysentery exudate from which he was able to isolate Shiga's bacillus, but he has never seen cysts of *E histolytica* in a bacillary-dysentery stool Other intestinal protozoa are encountered Sometimes the vegetative form of *E coli* may appear and these have to be differentiated from similar stages of *E. histolytica* The reader is referred to the Appendix, p 533, for details on this point During the stages of recovery intestinal flagellates such as *Chilomastix, Trichomonas*, and even *Giardia* may be present in considerable numbers It is probable that these organisms find in the bacillary-dysentery stool a medium which is congenial for their propagation, and it is probable, too, that their presence increases inflammation and irritation

Double infections of the amœba (*E. histolytica*) and the dysentery bacillus are not so common in Europeans as in debilitated, half-

cases no other bacillus was found so frequently in amœbic dysentery as *B dysenteriæ*, which was isolated from 27 out of 198 cases, also that in a number of fatal cases of chronic dysentery they found lung lesions due to *B. mucosus capsulatus*

Relationship of the pathological lesions to the presence of the dysentery bacillus —During the World War (1919) the author showed that the

4

dysentery bacillus could be isolated in the early stages directly from [illegible] place the organism

	Cases
Whole of the large intestine	24
Cæcum and transverse colon . . .	1
Rectum, sigmoid and transverse colon . . .	3
Rectum, pelvic colon and sigmoid . .	17
Sigmoid alone	5
Rectum alone	5

The tendency is for chronic bacillary ulceration to occur mostly in the lower part of the intestine, i.e in the sigmoid colon and rectum. In the upper portions ulcers are generally shallow and increase in depth and extent towards the lower portion. In two cases chronic bacillary ulcers were present in the lower part of the ileum, and the dysentery bacillus (*B flexneri*) was isolated

Histopathology.—The histology of the bowel in bacillary dysentery is a subject to which the author has given special attention and can best



P H M.-B.

Fig. 9.—Section of colon in acute bacillary dysentery (Shiga's bacillus), showing inflammatory reaction, especially in the solitary lymph follicle.

small hæmorrhages, the goblet cells being enlarged In the submucosa there is engorgement of the veins with considerable accumulations of inflammatory cells The inflammatory changes are most intense in the vicinity of the lymphoid follicles

In the necrotic stage the crypts of Lieberkühn's follicles are mostly destroyed, so that no definite structure can be distinguished. This layer has undergone coagulation-necrosis and is converted into a structure in which small hæmorrhages, accumulations of leucocytes



Fig. 10.—Microscopical section of the large intestine in bacillary dysentery
Showing necrosis of the mucosa, cellular infiltration, and hæmorrhages into the submucosa.

and pyknotic nuclei are visible. The muscular fibres of the muscularis usually escape. The submucosa is thickened to two or three times its normal width, distended with inflammatory exudate and the seat of numerous hæmorrhages. Chief features are thrombosis and the destruction of the blood-vessels, especially the veins. In the capillaries, it is

possible to recognize macrophage endothelial cells (histiocytes) apparently derived from the capillary endothelium. They are often large 15-20 μ in diameter, and contain ingested red cells, sometimes

necrosis.

Exfoliation of the necrotic mucosa is followed by granulation tissue, and the submucosa becomes the seat of newly-formed capillary vessels

In the stage of repair, proliferation of the columnar epithelium takes place from the fundi of Lieberkuhn follicles. The submucosa remains thickened and becomes the seat of fibrotic changes

Chronic ulceration—The formation of a chronic bacillary ulcer is illustrated in Fig 12 Ulceration proceeds from the fundi of the destroyed follicles, while fibrous tissue forms in the immediate vicinity. The formation of mucous retention cysts proceeds from the base of the Lieberkuhn follicles, forming cystic pseudo-adenomata distended with mucoid secretion At first they are lined by columnar epithelium, but later the cells are destroyed and the cavity is lined by basement membrane (Fig 8, p 41)

Symptomatology of Bacillary Dysentery

The practitioner in the tropics soon realizes that it is only in the acute and obviously toxic cases that his clinical acumen will permit a definite and positive diagnosis of bacillary dysentery. Even with the assistance of an efficient laboratory service, he must still be guided by clinical sense. When several cases of an acute dysentery of sudden onset with prostration and toxæmia occur in the same neighbourhood, and especially when children and the enfeebled are attacked, then a diagnosis of bacillary dysentery may with certainty be made; but it is all-important that, in every case, this surmise should have reliable laboratory confirmation Sporadic cases, and especially those not



Fig. 11.—Derivation of macrophage cells from the endothelium of capillary vessels of the submucosa in acute bacillary dysentery (Shiga's bacillus). Many of the cells have ingested red blood-corpuscles. (× 500)



Fig. 12.—Microscopic section of chronic bacillary dysentery ulcer (Flexner's bacillus) in the large intestine, showing structure

vomiting are noted The tongue is usually dry and furred and the pulse rapid and out of proportion to the degree of fever.

Incubation period.—Whenever bacillary dysentery appears in a crowded community it spreads with alarming rapidity. The incubation period, as determined by the experiments which have been undertaken on man in the few instances recorded, is generally from three to seven days According to Dudgeon the known incubation period in one case was twelve hours, in others thirty-two hours to six days In laboratory infections (Hirschbruck and H. Thiem) it is usually three days.

Onset—Symptoms usually begin suddenly; abdominal pain and discomfort with colic are felt some time before the initial diarrhœa begins, accompanied by violent and excessive peristalsis, and usually diarrhœa persists for a day or more before blood and mucus appear in the stool

E Becher (1918) considered that there are characteristic differences between the clinical course of Shiga dysentery and that due to Flexner, so that the latter is not to be considered merely as a slighter form Flexner dysentery, he thinks, begins quite acutely with a high fever of short duration, and simultaneously, or soon afterwards, diarrhœa sets in, with blood and mucus in the stools Rigors and vomiting are also often observed at the commencement of the disease which, on the average, runs a course of one week

[illegible], reach- [illegible] t, is of [illegible] rp rise [illegible] As a [illegible] tery is graver and the prognosis worse than in Flexner dysentery. This worker claims to be able to differentiate the two forms of dysentery on [illegible]

[illegible] there is an [illegible] flush which [illegible] æmia, while [illegible] is a feature of special note Usually there is a marked fall of systolic pressure, which for weeks remains below 110 mm. Hg.

Pyrexia.—Fever is an accompaniment of all cases of bacillary dysentery except in mild attacks. Generally it is of a low type, i.e.

from 99°-100° F (37 2°–38.8° C), but in the more acute cases the temperature rises to 103° and 104° F (39 4°–40° C.) at night The fever may be of an intermittent or even of a remittent type, and the

disease and the outlook then becomes grave

Abdominal pain and tenesmus, or straining —The griping abdominal pains due to violent and unrestrained peristalsis are very intense and distressing The pain is generalized over the whole abdomen, and attempts at palpation elicit tenderness, especially on deep pressure The area involves the small as well as the large intestine, while intense straining, or tenesmus, denotes that the pelvic colon and rectum are severely affected The spasm of the rectum may last for half an hour

is blunted by toxic absorption, prognosis becomes graver The spastic, contracted loop of the sigmoid colon becomes palpable and can be rolled like some pliable rubber cord beneath the examining hand In contrast to the amœbic form, transverse colon and cæcum are not contracted to such a degree and so cannot be readily discerned

Character of the stools —It would probably be more correct to describe the discharge from the bowel in bacillary dysentery as "exudate" rather than a stool The frequency and character of the evacuations may be taken as guides to the progress of the case In number they may vary in the twenty-four hours from two or three to fifty, or they may be uncountable, in other words, the unfortunate victim may be "glued to the commode"

In the early stages, during the first three days, evacuations consist of blood-stained mucus which is gelatinous and adheres to the bottom of the bed-pan or other container in appearance it has been variously compared to pink frog-spawn or to red-currant jelly It is practically odourless, or may give off a faint smell of spermin. After a period of three or four days the stools become more purulent, that is to say they

are mostly composed of pus cells, and blood is less apparent. In the next stage, bile pigments appear together with liquid grey fæcal matter; later still, during convalescence, the fæces become yellow or brownish.

The colour and consistency of the fæces, when the spasm of the sigmoid colon has passed off, vary considerably according to the diet Should the patient be fed on milk, solid casein curds [illegible]

is not necessary for the latter to be present before a diagnosis of bacillary dysentery be justifiably made. In the most acute and fulminating cases stools contain a large proportion of dark and decomposed blood They have been compared to "meat washings," exuding a kind of stale musty odour, or they may consist of blood-stained clots with a background of green, bile-stained mucus, betokening grave prognosis In very rapidly fatal cases no blood or mucus may be noticed in the stools from the commencement, but they consist of a foul fluid containing much altered blood but without admixture of mucus, unless one is familiar with the underlying pathology, stools such as these may be mistaken for ptomaine poisoning or some choleraic condition

The following table demonstrates in a dogmatic manner the main differences between the stool of acute bacillary dysentery and that of the corresponding stages of the amœbic disease.—

Acute Bacillary Stool	*Acute Amœbic Stool.*
Blood and mucus	Blood and mucus intermingled with fæces.
Mucus tinged with bright red blood throughout, viscid, adhering to bottom of pan.	Fluid mucus, not adhering to pan; blood generally dark red, in streaks or clots.
Odourless An acute inflammatory exudate derived from the mucosa of the whole or major part of the large intestine	Strong fetid odour, probably due to bacterial contamination and decomposing blood Derived from the sloughs of ulcers, together with *exudate and intermittent hæmorrhage.* Comparable with anchovy sauce

[illegible]

persisted for a considerable time [illegible] leucocytosis of from ten to fifteen thousand per cubic millimetre may

be present. Laempe (1918) records that there are usually about 13,000 leucocytes with a rise in the polymorphonuclears In the chronic form secondary anæmia is usually noted

Urine.—In severe cases the urine is of high specific gravity, about 1,030, concentrated, dark coloured, and contains a heavy deposit of urates. No albumin or any other abnormal constituent is present, except perhaps in the fulminating cases, where there is an increase of indican

Classification of the different types.—On clinical grounds the forms of bacillary dysentery encountered may be classified as follows: (*a*) mild, (*b*) acute, (*c*) fulminating, (*d*) relapsing, and (*e*) chronic

(*a*) *Mild or abortive type*—In the milder types, which are usually Flexner infections, constitutional symptoms are either entirely absent or not very severe, and there is no fever The motions may be composed of fæces from the commencement, or may contain a small quantity of blood and mucus

I [illegible]
twe [illegible]
felt [illegible]
rat [illegible]

[illegible]

caused by infections with either Sonne or Flexner bacilli

(*b*) *Acute type*—In acute cases the onset is much more abrupt Within a few hours the temperature may be raised to 101°–103° F. The patient is obviously suffering from intestinal toxæmia, for his face becomes pinched and anxious—manifestations of severe dehydration Defective absorption leads to chloride deficiency and tetany. Rigors are uncommon Mental confusion and slight delirium may at first [illegible]

[illegible]

fourteen days Anorexia is usually present The tongue is almost invariably coated with a thick yellowish fur, and the pulse-rate is accelerated, in fact, tachycardia is present out of all proportion to the pyrexia Tenesmus is a most distressing feature, especially during the night, and is usually accompanied by dysuria The abdomen is navi-

[illegible]

(c) *Fulminating or severe type.*—This includes the most severe infections and can be divided into sub-groups: (1) the choleraic, and (2) the

(1)

superf

obvio

with attendant phenomena setting in early, but may be more gradual with severe headache and anorexia The face is pinched, the eyes are sunken, and expression anxious, the temperature is subnormal, the *tongue dry and glazed the skin of the extremities cold and clammy* with tetanic cramps the pulse small, rapid and thready. The abdomen, at first acutely tender, becomes less so as toxæmia increases. Dysuria is usually acute *According to H Otto (1940), the facies Hippocratica*

more pronounced and death who resist the first three weeks, then

(2) The Gangrenous Form.—In this type the attack of dysentery commences suddenly, often accompanied by rigor, headache, vomiting, and other evidences of severe intoxication The temperature rises rapidly to 102° F (38 8° C) or even 104° F. (40° C). The face is flushed and feverish, the pulse, at first rapid and bounding, becomes weak and relatively slow, the blood pressure is so reduced as to register a

A particularly characteristic appearance is the passage of dark greenish sloughs, often of a considerable size, which represent the exfoliated and necrotic mucous membrane The stools are uncountable, with

tion of the
ere dysen-
the voice

Toxæmic nephritis, as described by N H Fairley in Pal stine, is accompanied by casts, high blood urea, and obvious signs of nitrogen retention

becomes husky, and collapse sets in. Severe cerebral symptoms are common, and psychoses were observed in the Polish epidemic (1939)

In this form the body may emit a musty odour, which becomes more intense as the disease progresses

[illegible]

were noted frequently during the 1914-18 War usually occurring at the advent of cold weather or as a sequel of some unaccustomed physical exertion Unless adequately treated, this type is apt to emerge into the chronic form

(e) *Chronic bacillary dysentery*—This form of dysentery in soldiers demobilized since the 1914-18 War received considerable attention They are victims of chronic ulceration of the mucosa, which has already been described Chronic bacillary dysentery is really a form of chronic diarrhœa with recurring exacerbations and occasional passage of blood and mucus, persisting for months, or it may be for years, and is particularly intractable

Diarrhœa due to chronic dysenteric infection has been recognized in India for many years under the synonym of *Morbus Bengalensis* (Chevers 1886), and accounts for an almost unbelievable emaciation in coolies in India and Malaya Intestinal symptoms may become exacerbated at intervals, sometimes with the passage of blood-and-mucus stools and chronic diarrhœa As the disease progresses, secondary anæmia becomes evident, with cardiac failure and œdema of the feet The sunken abdomen and extreme emaciation form a striking clinical picture Death usually occurs from exhaustion or from intercurrent disease, or may be due to hæmorrhage from the ulcers, while perforation of the bowel with peritonitis occasionally occurs The difficulties

[illegible]

bacillary dysentery commencing as a relapse after apparent recovery

Distinction must be made between the ulcerative and dyspeptic forms of bacillary dysentery. Some cases of chronic bacillary dysentery resemble ulcerative colitis, the patients continuously passing liquid fæces intermingled with blood and mucus The dyspeptic form is also fairly distinctive, and symptoms referable to disturbance of gastric function follow immediately upon the acute attack (see p 74)

Stenosis of the large intestine may take place as a sequel to chronic bacillary dysentery, but is rarer than is usually thought In one such case of the author's, narrowing of the lumen of the sigmoid colon was found

There is a form of chronic bacillary dysentery which closely resembles granular rectitis (see p 440) In this form the general condition of the

patient is good, but a granular zone extends 2-3 ins up the rectum, which has failed to heal The patient continues to pass blood and mucus after each formed motion. This condition may persist for more than a year subsequent to the acute attack of bacillary dysentery; it is usually amenable to bismuth subgallate retention enemata (*see* p. 453).

Special features of bacillary dysentery in the 1939-40 campaign.—In addition to the work of Otto and Gantenberg, K. Steuer (1940) has described special features of the epidemic of bacillary dysentery in the German Army during the Polish campaign. There were 1,200 cases, with 3 3 per cent mortality-incidence, and the epidemic was characterized by the rapidity of its spread The factors concerned in this are said to have been:—the endemicity of the infection, general lack of sanitation, mobile warfare, season of the year and contaminated water, added to flies and prolonged exhausting marches The inability, on account of existing conditions, to house the hospital staff in separate quarters, caused the infection of 5 out of 10 physicians, 4 out of 12 nurses and 8 out of 42 sanitary personnel.

In two-thirds of the series there was typical dysentery with bloody mucous stools In 26 6 per cent the condition was serious, in 6 6 per

infections pulse rapid and feeble, collapse frequent and not responding to medication Early death, usually in the second week, was associated with vasomotor paralysis

Only 9 out of 40 patients who died were received in hospital within 3 days of onset, but almost half were admitted after the first week; 80 per cent. of those re
within four weeks
18 5 per cent positi
Injection of antidy
circulation, pyrexia and tenesmus, and several subchronic conditions were benefited by serum enemata.

Complications were parotitis, disorders of bladder, rheumatic manifestations, conjunctivitis and intermittent fever. Pronounced arthritis was seen six times Œdema was frequently noted Major intestinal

populations can be formulated.

Bacillary dysentery in small children.—In the tropics bacillary dysentery is especially apt to attack small children under five years of age, and is to be regarded as a serious disease As a general rule it may be stated that it is much more acute and severe in European children than in those of native races The disease, apparently, can be spread by milk, which makes careful supervision and sterilization necessary. In young children the symptoms of toxæmia are much more sudden and acute, and may overshadow the bowel symptoms The attack may be ushered in with convulsions, and the child may die in coma

It has now come to be recognized that many of the epidemics of summer diarrhœa in the great cities of North America and Canada, even those of Europe, are due to infection with Flexner bacilli, therefore such cases should be recognized early and treated as if they were examples of bacillary dysentery Epidemic infantile diarrhœa is known in Japan as "Ekiri" This epidemic acute disease of infants, with sudden onset, fever, muco-diarrhœic sanguineous stools, cramps and collapse, prevails mostly in summer, sometimes in spring and autumn Death or recovery may follow within twenty-four hours of onset, and mortality varies between 39 and 82 per cent Sucklings are said never to be affected Possibly collapse may be ascribed to suprarenal insufficiency Treatment is by subcutaneous injection of adrenalin, 0 3 to 0 5 c c of 1 1000 solution, which is an effective remedy (K Kawata, 1925).

K. Kiyono and N Okubo (1917), M Minoda (1921), and S Tawara (1921) have written on this subject as it affects children from two to six years of age in Japan In these small children the dysentery toxin is especially apt to attack the central nervous system and the brain In about 1 per cent of cases Shiga's bacillus has been isolated, but K. Adachi (1921) has brought forward evidence that Sonne's bacillus

a mortality of 21 per cent Out of thirteen cases from which a satisfactory stool specimen was obtained, Flexner's bacillus was obtained in six, Shiga's bacillus in one Altogether, evidence of infection with *B dysenteriæ* of one kind or another was shown in 83 per cent of cases of clinical dysentery in hospital The ratio of Flexner to Shiga infections was 8 . 1

O Lade (1921) had the opportunity of studying 143 cases of bacillary dysentery in children in a clinic at Dusseldorf in Germany Thirty-three cases only were positively diagnosed and in 9 Shiga's bacillus was identified The seasonal incidence of bacillary dysentery in children was
October and i
took place
the first two

patient is good, but a granular zone extends 2-3 ins up the rectum, which has failed to heal The patient continues to pass blood and mucus after each formed motion. This condition may persist for more than a year subsequent to the acute attack of bacillary dysentery; it is usually amenable to bismuth subgallate retention enemata (*see* p 453).

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In two-thirds of the series there was typical dysentery with bloody mucous stools In 26 6 per cent the condition was serious, in 6 6 per cent extremely so, with cerebral involvement, pronounced dehydration, flabbiness of skin, cracked lips, brown discoloration of tongue and deeply sunken eyes Herpes of lips was common and hiccough always an unfavourable sign. Damage to circulation was seen with all serious infections pulse rapid and feeble, collapse frequent and not responding to medication Early death, usually in the second week, was associated with vasomotor paralysis

Only 9 out of 40 patients who died were received in hospital within 3 days of onset, but almost half were admitted after the first week; 80 per cent of those received within the first three days were discharged within four weeks Anal swabs (bacteriological tests) in 390 cases gave 18 5 per cent positive and 81 5 per cent negative for dysentery bacilli Injection of antidysentery serum produced therapeutic effects on circulation, pyrexia and tenesmus, and several subchronic conditions

heumatic mani-
iounced arthritis
Major intestinal

hæmorrhages resulting in anæmia were noted three times

Latent dysentery—J Cunningham (1918) concludes that a latent

populations can be formulated.

In Scottish asylums the disease appears to be rare, possibly because they are not so overcrowded

It is probable that in asylums epidemics are kept up by carriers, who are particularly difficult to detect Relapsing cases of dysentery are also probably responsible It was found at Claybury (London) that, out of 590 patients who have suffered from dysentery during the last twelve years, 18 per cent relapsed once, 6 per cent. twice, and 3 per cent three times

F H Lorentz (1913) gives an account of an outbreak of dysentery in the asylum at Duren, Germany, which was brought to a close by a systematic search for chronic carriers Four were discovered and by their isolation and the surveillance of all contacts, the outbreak was suppressed The uncleanly habits of the insane greatly facilitate propagation in asylums and, moreover, the type of dysentery is usually of a larval character, so as to escape early recognition The mortality is fairly high as the disease shows preference for old and debilitated patients

E T. Hilliard (1925) described bacillary dysentery as being endemic in the mental hospitals in Australia, at times flaring up into epidemics which are extremely difficult to eradicate The main clinical types to be distinguished were mild, relapsing, and toxic The organisms were isolated from the stools in 70 per cent of the acute cases, and proved to be Shiga 10 per cent, Flexner 30 per cent, and the Y bacillus 35 per cent The prevention of this disease in asylums consisted of quarantining newcomers for three weeks, and of the isolation of all cases of diarrhœa and dysentery, and carriers, for as long as possible

SHIP-BORNE DYSENTERY AND DIARRHŒA

The development of inter-oceanic and air-borne travel makes the subject of diarrhœa and dysentery contracted in transit a matter of importance and interest. This subject has attracted the notice of general practitioners during recent years on account of the increasing popularity of organized cruises to the tropics To some degree also the comparative cheapness of these tours has increased the opportunities to visit many hitherto unfrequented spots in the Ægean Sea, and has [illegible]
[illegible]
[illegible]
fly-borne or food-borne, of some meal eaten at a wayside restaurant, the most dangerous articles of food in this respect being fresh salads or fruits. Bacillary infection contracted on shore becomes manifest on shipboard two or three days after putting to sea

During 1936 a sustained correspondence on the subject appeared in the British Medical Journal J B Hern, in a somewhat alarmist article, described several hundred cases on a pleasure cruise of fourteen days' duration Dysentery with pyrexia (103° F) appeared forty-

G Kuntze (1921) records a summer and autumn epidemic of bacillary dysentery in 143 children, of which 85 were infants and 58 over eighteen months of age The clinical picture of the disease was by no means constant and the differentiation from the milder forms of diarrhœa was not generally easy

H Schelble (1918) studied the gradual spread of dysentery amongst the civil population in Germany during the 1914-18 War. In Bremen especially there was an increase of dysentery cases in the Children's Hospital From July to September, 1917, there were 82 cases with 21 deaths, a mortality of 25 per cent

Asylum dysentery.—Asylum dysentery can hardly be considered as a special clinical form of the disease, but for a long time it has been known that the form to which the feeble-minded are specially liable, in English and Continental lunatic asylums, is really a mild infection with dysentery bacilli, while attendants on these cases are apt to be attacked Acute and fulminating types are rare, and the chronic form is frequently encountered

In the majority of cases, according to H. S. Gettings, Flexner bacilli are responsible, but more recently Sonne's bacillus has been isolated Probably insanitary habits of the insane, their enfeebled constitution, and the breaking down of their natural resistance to disease are responsible for the spread of the infection The existence of bacillary carriers in most British asylums has been abundantly demonstrated.

In a report presented to Parliament in 1842, dysentery was recorded all over the Kingdom by the Poor Law Officers, with the sanitary zeal and reform of the 'fifties, the filth was swept away, and dysentery disappeared, to remain in the lunatic asylums

In 1911, there were in English asylums 1,457 cases with 313 deaths; in 1912, 1,555 cases with 287 deaths, in 1913, 1,159 cases with 270 deaths

During 1919 in eighty country asylums there were 1,722 cases, of whom 20 per cent died—forming 3 per cent of the total number of deaths Contrary to the generally accepted view that bacillary dysentery is a summer disease, the highest incidence of cases in Claybury occurred during the winter months

F. W. Mott in 1901 and 1902 made a careful study of the disease from a clinical and epidemiological viewpoint in this country

H S Gettings (1915) was able to trace the dysentery history of Wakefield Asylum (West Riding Mental Hospital, Yorks) since its opening in 1818 Almost from the commencement, dysentery made its appearance, and it has lingered on there ever since Sanitary



1 *P H M B*



2



3

1, Acute Shiga Dysentery, showing intense œdema of mucosa and submucous hæmorrhages in transverse colon. 2, Acute Sonne Dysentery in a child (Dr N. H. Fairley's case), showing bright pink hyperæmia of ascending colon 3, Ulcerative Colitis, showing destruction and ulceration of the mucosa, laying bare the muscular coat (lower sigmoid and upper rectum).

PATHOLOGICAL CHANGES IN THE LARGE INTESTINE

PLATE IV

eight hours after the commencement of the voyage. In the bacteriological investigation of one patient who had not recovered on her return to England, Flexner's bacillus was discovered; subsequently she suffered from two relapses.

stresses the difficulty of differentiating these cases from true bacillary dysentery, especially in the early stages.

The following is a summarized account of instances of this nature which have come under the author's personal observation:—

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1 200.

(b) A man of forty-eight, seen in November, 1935, on his return from Teheran, Persia, contracted bacillary dysentery and continued to pass blood and mucus on passage through Mediterranean. On arrival in England was still passing blood and mucus stools. Bacillary dysentery exudate; probably a *Flexner infection.*

(c) A man of thirty-one, seen on arrival in London in January, 1936, from a pleasure cruise from Aden, where he apparently contracted bacillary dysentery, which became apparent in the Red Sea, three days out. Pyrexia, blood and mucus in stools. Was treated as a case of amœbic dysentery. No evidence of this infection ever obtained. On arrival in England stools still contained blood and mucus. Serum agglutinated *Flexner's bacillus* 1 : 800.

(d) A retired Colonel, aged sixty-nine, had been on a trip to Khartoum. Developed acute dysentery on Nile steamer and was extremely ill at Juba. Flown to Entebbe by air, and treated as case of acute amœbic dysentery, with emetine injections. Became very emaciated and extremely ill. Arrived in Eng

(e)

on th

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out at sea. On board ship he was treated as a case of amœbic dysentery, with emetine injections. On arrival in London was passing blood-and-mucus

she contracted some form of acute dysentery in May, 1934 Treated as amœbic dysentery with emetine injections Dysenteric attacks, accompanied by pyrexia Loss of 14 lb in weight Relapse on board ship Fæces contained blood and mucus, bacillary dysentery exudate. Serum agglutinated *Flexner bacillus* 1 200

Some cases are doubtless due to Sonne's bacillus, and the danger of food-borne infection on shipboard has not been sufficiently recognized

In March, 1934, the author investigated the case of a woman who had developed dysentery, with passage of blood and mucus, on board ship, and had suffered from three distinct attacks, with some pyrexia [illegible] Her boy of three, who shared [illegible] The fæces of both consisted of a [illegible] The serum of both agglutinated [illegible]

The author has seen a good many cases of white diarrhœa with sprue-like stools commencing on board ship The other accompaniments of sprue, such as wasting, sore tongue and anæmia were absent In one instance it was ascertained that the original infection was Sonne's bacillus, which, it must be noted, may produce a clinical condition simulating temporarily the clinical features of sprue This by no means [illegible] sprue-like diarrhœa and characteristic stools The illness commenced ten days after leaving Japan and persisted throughout the voyage

Other cases of ship diarrhœa resemble mucous colitis (*see* Chapter XXIII) and may be the sequel of a bacillary-dysentery infection contracted on shore A similar form is also frequently seen in small children. [illegible]

affection has a disturbing effect upon temper and mentality, the children becoming a trial to their parents The exacerbation which becomes apparent on the voyage may be due to unsuitable dietary, though change in temperament and appearance when on a fat-free diet is remarkable

The author has not encountered amœbic dysentery contracted at sea, but he has seen many instances where the infection was acquired ashore, and gave rise to symptoms for the first time on board ship These patients, as a rule, contracted the original infection in India and the Far East

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Other cases of ship diarrhœa resemble mucous colitis (*see* Chapter XXIII) and may be the sequel of a bacillary-dysentery infection contracted on shore A similar form is also frequently seen in small children The author's experience also points to the possibility of cœliac disease making its first appearance in children from the tropics when on board ship. The clinical appearance of these children is quite characteristic, with pasty complexion and turgid swollen abdomen The cœliac affection has a disturbing effect upon temper and mentality, the children becoming a trial to their parents The exacerbation which becomes apparent on the voyage may be due to unsuitable dietary, though change in temperament and appearance when on a fat-free diet is remarkable.

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SONNE DYSENTERY

A full account of the bacteriology of Sonne's bacillus is given in the Appendix (p. 561).

Recent work on Sonne infections in England and other countries has brought to light a new clinical entity. Particular prominence is given to the very varied clinical pictures which this bacillus may provoke, and which differ in many respects from the clearer-cut dysenteric [illegible]

cases. In the early stages the fæces are greenish, with blood-flecked mucus from which almost pure cultures of late-lactose-fermenting organisms (Sonne) may be obtained. Confirmation of their identity with specific serum is readily produced.

[illegible]

mucoid stools.

In all Sonne infections there is a tendency to pyrexia associated with [illegible]

apyrexial Sometimes pyrexia may be due to superimposed causes, such as mastoiditis or appendicitis. Intestinal symptoms are not [illegible]

stools remain loose and greenish, but in the next few days become brown, formed and more normal.

E Harvey has reported that very acute Sonne infection in children up to nine years of age may be the cause of sudden death

The paper by J A Charles and J H. Warren (1929) indicates how widespread this infection may be in England as a result of acute attacks of "food poisoning," a point to which W G. Savage and P. B White first drew attention in 1928. An outbreak described by R E Smith is interesting because some cases were of this acute type

One of the best-described outbreaks of food poisoning due to Sonne's bacillus occurred in St Pancras and Holborn, London (G Snowden, 1938) Here 13 people were attacked, 11 in St Pancras and 2 in Holborn Five were adults, eight children, and two of the latter, aged 11 and 13, died.

The clinical symptoms were vomiting, acute abdominal pain with [illegible]

and bacteriological examination revealed large numbers of Sonne's bacilli At the inquest it was ascertained that about twenty people had partaken of it and the evidence proved, as far as proof was possible, that a girl, who was found to be a carrier, had contaminated the pudding

A M Fraser, J. P Kinloch, and V J Smith (1926), in the routine examination of enteritis cases in Aberdeen, found 83 of Sonne dysentery, most of them in institutions where the inmates were under strict medical observation The blood serum of 81 cases, taken between seven and twenty days from the onset, gave a positive agglutination in dilutions varying from 1 50 to 1 6,400

G M Fyfe (1927) has described a milk-borne epidemic of Sonne dysentery at St Andrews between September 5 and September 26 The total number of cases was estimated at nearly 200 and there were no fatalities The incubation period was shown to be probably less than twelve hours The respiratory catarrh which was such a feature of the Aberdeen outbreak was not noticed Usually recovery was complete in a week

A similar outbreak has been described by G Abraham (1929) in seventy cases in Frankfurt-on-Main Toxic symptoms in the form of unconsciousness, convulsions, and delirium were present

The year 1937 witnessed a remarkable increase in the number of dysentery cases of the Sonne type in this country, recorded in many quarters, but mostly in the London area Possibly this was due to the improved methods of diagnosis and the more general appreciation of Sonne's bacillus as a pathogenic agent

There has been a general increase in the figures in the Registrar-General's weekly return for the last few years but towards the end

of 1937 a very marked increase was noted; for the week ending December 4, 1937, there were 454 cases. The figures for 1935 and 1936 were *double and treble those for 1934, while those for 1937 were ten* times that number. In passing, it should be remarked that, judging from the returns of the Health Section of the League of Nations, the same tendency to increase is shown in many European countries; in Germany, for instance, the summer figures for 1937 are almost double the mean values. E Bloch (1938) has drawn attention to the great increase in Sonne dysentery in Glasgow in institutional as well as non-institutional environments. Towards the end of 1937 the first large outbreak of this type of dysentery was recorded. Most of the cases were very mild

The last two years (1939–41) have witnessed further widespread epidemics in England, and it has proved a definite factor in dysentery outbreaks in the Middle East

Fæces + and rectal swab +	36
Fæces —, rectal swab +	34
Total fæces +	45
Total swabs +	70

carriers play an important part in the spread of infection. Three negative swabs are necessary before discharge. Serum agglutination tests have a definite diagnostic value in a fair proportion, but repeated ... shown conclusively that sera initially negative remained so

were isolated from the milk, as well as from the fæces of the patients. Fifty-nine out of 106 households were affected.

Complications of Bacillary Dysentery

Dysenteric arthritis.—This complication appears to have been [illegible] ed it "*rheumatismus intestinalis*" [illegible] of physicians in India it was [illegible] In many respects dysenteric arthritis resembles that of gonorrhœa, and it is a curious fact that it is common in some epidemics and rare in others. In the Doberitz epidemic in Germany in 1900, arthritis developed in 8.75 per cent. of all cases, in 1897 in a similar outbreak in the Fiji Islands (C. W. Daniels) [illegible]

Usually dysenteric arthritis is associated with Shiga toxins, but in some cases a Flexner infection has also been noted, but there are no records of it in the Sonne disease. The joint affection rarely develops in the acute stage of dysentery.

[illegible]

of opium were the most apt to develop arthritis.

An interesting fact is that there appears to be no correlation between the intensity of the arthritis and the severity of the initial dysentery. G. Graham (1919) believes that patients who show symptoms of arthritis early are more liable to severe attacks: [illegible]

left thigh.

Occasionally the temporo-maxillary and sterno-clavicular, and very rarely the hip-joints, suffer. The affection usually flits from one joint to another with short intervals between. Different types of joint affection may be distinguished. The pains may be evanescent, and it is possible that the arthralgia is often situated in the fibrous muscle insertions.

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organisms in the stools without showing any clinical symptoms. In mental asylums both these forms of "carrier" play a considerable part in spread

bacillus

within a

The la

epidemics in England, and it has proved a definite factor in dysentery outbreaks in the Middle East.

Fæces + and rectal swab +	36
Fæces —, rectal swab +	34
Total fæces +	45
Total swabs +	70

carriers play an important part in the spread of infection. Three

pigment arranged fringe-wise round the margin of the membrane and also extending along those lines running radially between it and the edge of the iris.

There is acute tenderness on pressure over the ciliary region, with photophobia, blepharospasm, and marked circumcorneal hyperæmia The pupils are irregular with ring synechiæ. Iridectomy was performed in one case and the aqueous humour was found by J. A Arkwright to agglutinate Shiga's bacillus 1 80 G Worms, P Lesbre and G Sourdille (1926) noted that, in dysenteric sclero-conjunctivitis, the tears did not contain specific agglutinins As a rule, iritis subsides *pari passu* with arthritis

Parotitis.—This may be either uni- or bi-lateral, is painless, and is usually associated with joint complications It is difficult to say whether it is of true dysenteric origin or whether it is due to septic absorption from the mouth A particularly severe form ending in gangrene has been observed in Sumatra by J Smits (1915)

Portal thrombosis.—This has been recorded and has led to portal pyæmia and miliary abscesses

Intussusception.—Intussusception of the small bowel may occur in bacillary dysentery in children It is very necessary that this com-

dysentery and is frequently mistaken for it, and is also found post

its enfeebling

ic movements,

Thrush.—In the tropics, infection of the mouth, the pharynx, and even the œsophagus, with the greyish growth of the thrush fungus is common, and in these cases large numbers of the characteristic yeast cells are present in the stools, and may cause them to assume a frothy bubbling character somewhat resembling those of sprue

SEQUELÆ OF BACILLARY DYSENTERY

Peripheral neuritis may follow bacillary dysentery, as many other specific infections This has been doubted, but the author has seen so many cases following on dysentery epidemics that he is inclined to believe there is some connexion. The legs are usually affected, with loss of knee-jerks, glossy, atrophic skin, œdema of the ankles, and hyperæsthesia of the calves This condition may persist for several months

A. Dittorf (1918) observed neuritis in 1 per cent of cases in an *extensive epidemic*; *he regarded it as a secondary toxic affection due*

Hydrarthrosis.—In the knee a large effusion of synovial fluid may occur suddenly—it may be into the subcrureus pouch. The author noted that this is more likely to occur in rheumatic subjects. The effusions are usually accompanied by a rigor, by a rise of temperature to 102–103° F. (38·9–39° C.) and, in the initial stages, by pain, which, however, soon wears off, leaving stiffness, while the skin over the affected joint is shiny and reddened.

When aspirated, the inflammatory fluid is straw-coloured, slightly viscid and usually sterile on culture, and it has the important property, as noted by B. G. Klein (1919) and S. H. Zia and H. J. Smyly (1931), of agglutinating the infecting dysentery bacillus (Shiga or Flexner) in a titre higher than that given by the blood-serum from the same case. Apparently the joint effusion never becomes purulent, nor are the heart or valves ever affected.

There is some evidence, as noted by the author, that arthritis is more likely to develop in serum-treated cases, and it becomes necessary to distinguish between dysenteric arthritis and fugitive poly-arthritis which may accompany serum sickness (P. Manson-Bahr, 1920; Z. Cope).

Dysenteric arthritis involving many joints may persist from a few days to six or eight weeks, but, however alarming this condition may appear at first to the patient and his medical attendants, it is comforting to know that permanent disability seldom ensues. Some disability is produced by the stretching of the joint capsule and the surrounding ligaments but, according to G. Graham, complete recovery may ensue even after this has persisted for six months.

In 1920 the author recorded arthritis associated with large, sterile effusions into the glutei and latissimus dorsi muscles which subsided slowly.

and may eventually lead to a more intractable disability.

to absorption of bacteria and their toxins from the ulcerated bowel. Malnutrition and emaciation, which cause the disappearance of fat from the medullary sheath of the nerves, favour it. The majority of cases exhibited mainly sensory disturbances, partly subjective and partly objective, without trophic changes Muscular spasm and cramps, especially of the calf muscles, were not rare, and only one case of severe motor neuritis had been seen

A G Biggam (1929) recorded a case in which the sequence of events appeared to suggest that acroparæsthesia of the legs was due to dysenteric toxins Rapid improvement followed on large doses of intravenous antiserum

Stenosis.—Stenosis is the result of great damage to the mucous

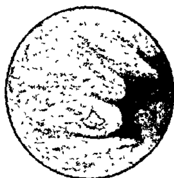
only in thirty years' experience in India, and the author has encountered one single instance as the result of infection contracted during the 1914-18 War.

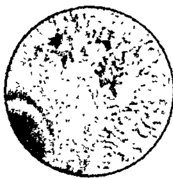
Post-dysenteric constipation.—This is frequent after the subsidence of an acute attack, and is possibly due to the resulting atony

Hæmorrhage.—Massive intestinal hæmorrhage from ulcers has been recorded in the chronic form

troubles following bacillary dysentery. In the author's series of post-bacillary dyspepsia, achlorhydria and hypochlorhydria have been found to be the rule.

Tachycardia.—Owing to the physical exhaustion of the patient, and possibly also to toxic myocarditis, a condition of irritable heart persists long after dysenteric symptoms have disappeared. In those cases in which a record of the pulse-rate has been kept during convalescence, it has been shown that tachycardia becomes more

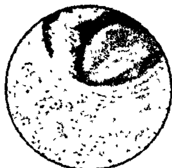












P. H. M. B.

SIGMOIDOSCOPIC APPEARANCES

PLATE V

PLATE V

SIGMOIDOSCOPIC APPEARANCES

A. **Amœbic Ulceration** of lower rectum, giving rise to symptoms suggesting carcinoma

B. **Intestinal Bilharziasis.**—Early stage. Patches of granulation tissue containing eggs of *Bilharzia mansoni*

C. **Chronic Bacillary Dysentery Pseudopolyposis.**—Flexner Y infection Agglutination test positive to Flexner 1 1:80 Great improvement on intestinal lavage

D. **Acute Amœbic Dysentery**—Active ulceration of mucosa with blood and mucus exudate

E. **Acute Bacillary Dysentery**—Shiga's bacillus isolated. General œdema of mucosa, spasm, submucous hæmorrhages Early healing stage.

F. **Amœbic Dysentery.**—Chronic stage, showing "pitting" of mucous membrane

Peritonitis.—Acute perforation of the large intestine has been recorded by N. H Fairley recently in three cases in the Middle East. Localized subacute peritoneal effusions, with adhesions in the right iliac fossa, have also been described in the chronic form Massive serous peritoneal effusions have also been observed in toxic cases not responding to treatment

Post-dysenteric ascites.—J W D Megaw and G C. Maitra thought that the ascites which is so commonly found in India in association with conditions of the liver is a sequel to repeated infection Whenever bacillary dysentery is improperly treated, the dysenteric toxins pass through the intestinal walls and give rise to an irritative peritonitis which is followed by fibrosis of the peritoneum, with resulting ascites

Ascites is more likely to occur amongst patients who continue to be carriers , among such cases, therefore, agglutinins in the serum are more likely to persist than among an average series of recovered bacillary dysentery.

Other diseases.—Other infections of the colon, such as amœbiasis, may follow on a bacillary attack Tuberculosis of the large bowel has also to be considered, as well as sprue in Eastern countries, and that particularly distressing complaint, mucous colitis These sequelæ will be dealt with under their appropiate headings

be observed, with sloughing of the necrotic mucosa The patient usually, at this stage, shows evident signs of toxic absorption

In acute bacillary dysentery of a milder type (caused by Flexner [illegible]

mucosa, and the superficial necrotic mucous membrane may be visualized as a thin greyish layer exposing a red, raw and bleeding surface when removed The bowel wall, at this stage, is usually rigid and inelastic

When cases are repeatedly examined, exfoliation of the superficial necrosis can be seen, the bowel gradually resuming its normal appear-



Fig. 13.—Sigmoidoscopic appearances of chronic bacillary dysentery (left) and [illegible] (right)

ance Much viscid mucus is secreted by the bowel during the healing process

In *convalescent bacillary dysentery* the mucous membrane is nodular, rose-pink or bluish-red, and œdematous Numerous red blotches are interspersed, caused by submucous hæmorrhages The walls of the bowel are rigid and inelastic and the natural folding is absent The mucosa is readily traumatized and the lumen filled with blood-stained mucus

In the *subacute stages* the bowel surface is covered with granulation [illegible]

granular mucosa bleeds readily (Fig 13) Scrapings reveal numerous

CHAPTER VIII

THE BACILLARY DYSENTERIES (*continued*): DIAGNOSIS

It has frequently been emphasized that in bacillary dysentery it is unwise entirely to rely on a clinical diagnosis. The acute and fulminating types of the disease are obvious, but in less marked forms difficulties arise. In making a laboratory diagnosis it is necessary that the pathologist should have had the benefit of considerable experience of this highly specialized work, for bacillary dysentery frequently occurs as a terminal infection in chronic wasting diseases such as pellagra, phthisis, kala-azar, bilharziasis, amœbic dysentery and scurvy Long-sustained pyrexia may be due to superimposed paratyphoid infection In chronic cases, persistent pyrexia and frequent rigors may be due to *B.-coli* septicæmia or malaria. *Malaria* in dysentery is a serious complication, specially apt to appear because dysentery in a malarial subject may light up a smouldering infection. On the other hand, it may co-exist with primary subtertian malaria, in which case it is just as important to treat the latter as the former. *Pneumonia*, either of the lobar or broncho-pneumonic type, is a frequent terminal event in the more chronic form.

DIAGNOSIS BY SIGMOIDOSCOPY

introducing the instrument may be acute, and damage may result,

certainty.

The appearances at the early and acute stages, which have been described so ably by A. G. Biggam (1930), resemble very closely those

mucosa, white granulations appearing as a delicate network, or more widely spaced

Melanosis coli.—Melanosis coli is a curious condition of melanin-pigmentation of the rectum and sigmoid, the nature of which is obscure The author has seen this in three patients who had suffered from bacillary dysentery and consequent diarrhœa over a long period (Fig. 14)

Attention was originally drawn to pigmentation of the colon in dysenteries by A L. Gregg (1923) and was attributed by him to the [illegible]

X-RAYS IN DIAGNOSIS

[illegible]

and are indistinguishable from similar appearances in chronic ulcerative colitis (Plate I, p 42)

LABORATORY DIAGNOSIS

In hardly any other disease is it so essential that attention should be given to details of laboratory technique, since the symptoms of bacillary dysentery may be simulated by so many other causes of intestinal ulceration that the final diagnosis must always depend upon the pathologist, and since it is essential, in the interests of the patient, that appropriate treatment should be given at the earliest possible moment

Direct microscopic examination.—A provisional diagnosis of bacillary dysentery can be made by examination of the cellular exudation, and for this two conditions are absolutely necessary (1) that the specimen has been freshly passed, and (2) that it is passed early in the course of the disease. The stool should be collected in a bed-pan and brought direct to the laboratory

The selection of a portion of the stool suitable for microscopic examination or culture should be made by the pathologist It must be emphasized that, in both the bacillary and the amœbic form, all diagnostic features may disappear after a lapse of from four to six hours, and this is especially likely under tropical or subtropical conditions So

pus and macrophage cells The exact appearance of the bowel varies in different stages; sometimes a pseudo-polypoid condition is simulated by the heaping up of exuberant granulation tissue (Plate V, B); sometimes fibrosis of the bowel wall may result in partial stenosis or fibrotic scarring. The patulous condition of the anus and atrophic appearance of the skin surrounding the anal margin, together with the wasting of the gluteal and perineal muscles, afford a considerable amount of additional evidence in diagnosis.

H. J. Smyly (1930) has emphasized a point which the author has often observed, namely, that there is in milder forms of chronic bacillary

Fig 14 —Sigmoidoscopic appearance of *Melanosis coli*, showing pigmentation of colon sometimes found as a sequel to chronic bacillary dysentery. P H M-B

dysentery, a hyperplasia sufficient to obscure the small blood-vessels which are normally visible.

Some of Smyly's cases presented ulcers in the rectum or sigmoid or both. The commonest type is a very shallow ulcer, the margin of which is sharply defined, and ranging in size from one millimetre or less to over a centimetre. The base is usually covered with pus, which is easily swabbed away, exposing red granulation tissue. Another type of ulcer resembles a crater umbilication, or a well-defined papule. By cultures from the surface of th[illegible] swab, a growth [illegible] with a toothpick

A [illegible]

dysen[illegible] the rectum, is a [illegible] in chronic bacillary [illegible] tessellated pattern on a red

mucosa, white granulations appearing as a delicate network, or more widely spaced

Melanosis coli —Melanosis coli is a curious condition of melanin-pigmentation of the rectum and sigmoid, the nature of which is obscure The author has seen this in three patients who had suffered from bacillary dysentery and consequent diarrhœa over a long period (Fig. 14)

Attention was originally drawn to pigmentation of the colon in dysenteries by A. L. Gregg (1923) and was attributed by him to the [illegible]

laxatives when used over long periods, and they have found that these aperients contain resinous substances and some pigment matter which is intimately associated with active aperient principles The deposition of this pigment in the mucosa produces melanosis

X-RAYS IN DIAGNOSIS

[illegible]

LABORATORY DIAGNOSIS

In hardly any other disease is it so essential that attention should be given to details of laboratory technique, since the symptoms of bacillary dysentery may be simulated by so many other causes of intestinal ulceration that the final diagnosis must always depend upon the pathologist, and since it is essential, in the interests of the patient, that appropriate treatment should be given at the earliest possible moment

Direct microscopic examination.—A provisional diagnosis of bacillary dysentery can be made by examination of the cellular exudation [illegible]

features may disappear after a lapse of from four to six hours, and this is especially likely under tropical or subtropical conditions So

important is the collection of suitable material that some pathologists now prefer to obtain the blood and mucus direct by the rectal swab method (*see* p 70). However obtained, a portion of the blood-stained mucus should be placed by means of a platinum loop on a clean glass

Cellular exudate—The most characteristic feature of the bacillary dysentery stool under the microscope is the very large proportion of polymorphonuclear leucocytes Red blood-corpuscles, too, are very numerous and, excluding these, pus cells constitute quite 95 per cent. of the exudate It has been noted by J G. Willmore, C. H. Shearman (1918), and others, that these polymorph cells possess distinctive ringed nuclei, due to the accumulation of chromatin on the periphery of the nucleus, they have been appropriately termed "ghost cells."

Macrophage cells—In addition to the polymorphonuclears, a much larger cell, which seems to be characteristic of bacillary dysentery, occurs at an early stage The appearance of these cells in the stool and their characteristic refractivity have given rise to confusion in diagnosis, so that it is permissible to emphasize their importance The macrophage (histiocyte) is a cell usually 10–45 μ in diameter, apparently derived from capillary endothelium (Fig 11, p 55), constituting about 2 per cent. of the cellular exudate. It may be round, oval or even bilobed In its cytoplasm it contains vacuoles and granules of various kinds, fat globules, and sometimes even ingested red cells, or leucocytes. Those globules, of greenish colour, consist of chromatin due to the destruction of the nucleus, and others consist of fat due

are, however, defunct and therefore non-motile, and, to the practised

as well as mononuclear leucocytes and lymphocytes. Eosinophils are rarely encountered

TABLE VI

Differentiation of Bacillary Dysentery and Amœbic Dysentery Stools by the Cellular Exudate

	ACUTE BACILLARY DYSENTERY	ACUTE AMŒBIC DYSENTERY
Red cells	Numerous and scattered throughout preparation	Numerous, occur in clumps and rouleaux
Polymorphonuclears	Numerous with clear cut ring nuclei	Undamaged cells extremely scarce, those which occur have eroded margins
Nuclear masses	Free from cytoplasm, scarce	Free from cytoplasm, very common
Macrophage cells	Large and numerous, containing ingested red cells	Rarely seen
Eosinophil cells	Scarce	Numerous
Epithelial cells	Common, generally bile-stained and disintegrated	Numerous and apparently undamaged
Bacilli	Extremely scarce	Motile and in large numbers
Entamœba histolytica	Absent	Present

The following summarizes the relative percentages of cellular constituents of the stools in bacillary and amœbic dysentery —

TABLE VII (J Anderson, 1921)

	BACILLARY DYSENTERY	AMŒBIC DYSENTERY
Polymorphonuclears	90 7 per cent	7 5 per cent
Mononuclears	1 01 ,, ,,	0 7 ,, ,,
Lymphocytes	2 8 ,, ,,	2 5 ,, ,,
Eosinophils	0 01 ,, ,,	3 2 ,, ,,
Macrophage cells	1 8 ,, ,,	0 ,, ,,
Epithelial cells	1 48 ,, ,,	1 3 ,, ,,
Plasma cells	1 61 ,, ,,	1.8 ,, ,,
Nuclear masses	0 ,, ,,	83 ,, ,,

attention to their superficial resemblance to amœbæ and the likelihood of the pathologists mistaking them for these protozoa, especially in sections.

The author (1912), in his work on dysentery in Fiji, once more called [illegible]

1914-18 War

This subject assumed greater importance during the epidemics of dysentery in Gallipoli in 1915, mainly because of the *imprimatur* conveyed to it by the work of G B Bartlett (1917) in his report to the War Office In this paper it became apparent that macrophage cells (histiocytes) had been confused with stages in the life-history of *Entamœba histolytica*. The question was [illegible]

size from 25–45 μ, and as being non-motile, with densely granular cytoplasm and a large ring-form nucleus He rightly considered them to be endothelial phagocytes and similar to large wandering body-cells.

[illegible]

J Anderson (1921), working in the author's laboratory in Palestine, made differential cell-counts of the cellular exudate in the two diseases. J. G. Thomson and A. Robertson (1921) gave a series of figures illustrating the morphology of the inflammatory cells in the exudate.

This was followed in 1924 by a monograph by F. G. Haughwout in which the importance of cytodiagnosis was perhaps over-emphasized. He concluded that in bacillary dysentery the cellular exudate is characteristic of that condition and of no other intestinal disorder The phagocytic endothelial cells and the annular degeneration of the nuclei of the polymorphonuclear pus cells are considered pathognomonic, on the other hand, he held that "ghost cells" and endothelial cells are absent in acute amœbic dysentery and in balantidiasis

Finally A Alexeieff (1927) repeated with elaborate care the researches already outlined, and reached much the same conclusion He emphasized the importance of the macrophage cells (plasmophages) which are found in abundance in the mesenteric glands of acute bacillary dysentery cases as well as in the exudate.

The proportion of Shiga to Flexner bacilli isolated from the stools during the course of an epidemic —It has frequently been pointed out that at the com-

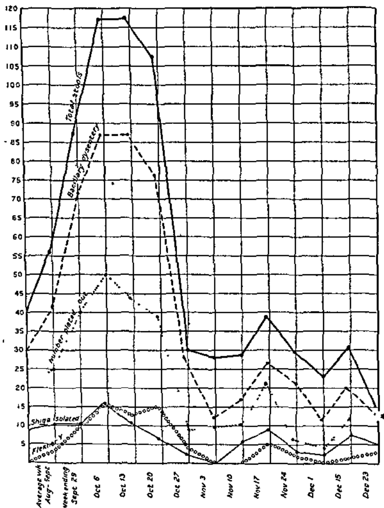


Chart 1.—Illustrating the proportions of positive stool cultures obtained under war conditions to the number of "dysentery" fæces examined (1917). * Denotes the number diagnosed bacillary dysentery on the cellular exudate.

(Manson Bahr, *Jour R Army Med Cps*, Aug, 1919)

The total number of stools examined during this period was 837, and in 664 of these the specific cause could be ascertained.—

(1) 6 (0 9 per cent) were associated with *Giardia intestinalis*; (2) 11 (1.6 per cent) with flagellates—*Trichomonas* or *Chilomastix*; (3) 7 (1 05 per cent.) with *E. histolytica*, (4) 633 (95 3 per cent) were diagnosed in the cellular exudate as *bacillary dysentery*; (5) 342 (51 per cent) were plated out; (6) in 201 (59 1 per cent) dysentery bacilli were isolated; (7) in 114 (33 5 per cent) Shiga's bacillus; and (8) in 87 (25 4 per cent) Flexner-Y bacillus

In any large epidemic, bacilli of more than one type are found and a pure Shiga or a pure Flexner epidemic appears to be a rarity. In Salonica, L. Dudgeon (1918) obtained the following figures:—

	Cases	*Percentage*
Shiga B	335	38 3
Flexner B ...	503	57 3
Other Types ..	36	4 1

D Graham and his collaborators (1918) obtained much the same figures in 2,500 cases.

[illegible]

reached by the instrument.

Examination of material obtained by rectal swabs.—*During the 1914-18 War, on the Western Front, this method was* extensively used for obtaining suitable material for culture from the lower rectum, and the results are more satisfactory than those obtained [illegible] e has also borne

long by 2 cm.
Situated 8 cm.
above the lower end, which is closed as in a test-tube, is a circular [illegible]

[illegible]

The reader is referred to the Appendix, p 550, for further details

of the technique of isolation of the organisms and the types of media employed.

Methods employed in chronic bacillary dysentery.—In the author's series of 107 cases of chronic bacillary dysentery in the Hospital for Tropical Diseases, London, during the years 1920–37, the great majority were diagnosed by sigmoidoscopic appearances, 21 were diagnosed by the agglutination test; 12 by sigmoidoscopy as well as by the agglutination test, but only 3 by actual isolation of Flexner's bacillus from the fæces

Serological diagnosis.—It cannot be sufficiently emphasized that accurate diagnosis is of paramount importance in the differentiation of the dysenteries; therefore, every means must be brought to the aid of the clinician in a particularly difficult case. It is a matter of considerable disappointment that serological diagnosis, usually so satisfactory in the typhoid group, is such a comparatively unreliable weapon in bacillary dysentery

In the first place, some normal sera have a definite action upon freshly prepared emulsions of dysentery bacilli (A D Gardner, 1923) It has already been emphasized that only the macroscopic method is suitable in dealing with these organisms The best results can be obtained by using Dreyer's technique with definitely sensitive agglutinable emulsions It is the general opinion that in Shiga infections a positive diagnosis can be accepted when the titre is as low as 1 40, but with the Flexner group agglutination should take place in a dilution of 1 : 100 The difficulty of obtaining positive results in certain circumstances arises not so much with Shiga as with Flexner

homologous suspension for agglutination

There are fallacies in the use of the agglutination test in this connexion which may be stated as follows It is difficult to accept a negative test as being of value unless it is made after the eleventh day of the disease The agglutinins appear generally about the seventh and reach their maximum about the twenty-first day and then show a rapid decline A previous attack of bacillary dysentery may have to be taken into account, as residual agglutinins may persist in the serum for a considerable time—it has been stated that these can be demonstrated after as long an interval as three and a half years The limitations of this test, therefore, are very obvious, and in those acute cases in which a rapid diagnosis is very urgent it is, unfortunately, of little value.

The agglutination test as an aid to diagnosis was originally investigated by the author in his work on dysentery in Fiji in 1912 The microscopic test alone was utilized, with culture isolated from actual dysentery cases under treatment. The sera of 112 cases were tested A positive agglutination

the serum

The highest agglutinin titres were encountered during the second and third weeks of the disease No agglutinins were found before the fourth day. *In a Flexner infection it is necessary, according to modern knowledge, to* employ at least five separate serological stains of Flexner antigens, for the results obtained with one differ from those obtained with another.

The conclusions arrived at are that the agglutination test is a

…ory, but the

…ciated with

…nin content

…ever, more

satisfactory and consistent results have been obtained by employing a pooled antigen of the different types described by Boyd (1939) (*see* p 561). He emphasizes that smooth specific cultures must be used *and this applies especially to Schmitz and Sonne bacilli.*

In cases of "clinical" dysentery (i e, cases in which bacteriology of the fæces has given no assistance) in which the Shiga reaction is negative on the first occasion, although a reaction to Flexner has been recorded, it is necessary to repeat the examination seven days later with Shiga and Flexner antigens, as by this time a Shiga reaction may have developed.

… have contributed to this subject by

In chronic cases of bacillary dysentery a definite result may be obtained

of strains and it is almost impossible to prepare suspensions which are free from group antigens Furthermore, serum from normal individuals and from normal rabbits frequently contains a considerable concentration of natural agglutinins for these group antigens

Serological properties of dysentery stools—A Davies (1922)

adopted to ascertain the presence and titre of agglutination was that of Garrow (*see* Appendix, p 565) The method is especially valuable in Shiga infections, and in chronic cases it was found particularly helpful, the specific agglutinins being obtained from pledgets of mucus passed in the fæces

Examination of the blood—G M Findlay (1919) found that assistance can be obtained in differentiating bacillary from amœbic dysentery by the reactions which occur in the polymorphonuclear leucocytes—the iodine reaction and the production of nuclear pseudopodia He considered that an accurate diagnosis of the type of dysentery can be given at an early stage of the disease A well marked iodine reaction without the formation of nuclear pseudopodia suggests a bacillary infection the presence of nuclear pseudopodia with absence of the iodine reaction indicates amœbiasis

Intradermal reactions.—H Brokman (1923) applied the Schick

antidysenteric serum

C Zoeller (1927) has also described a similar reaction He uses 0 2 c c of a 1 100 dilution of dysenteric toxin The specific reaction does not appear till the third or fourth day, when an ecchymotic tinge becomes pronounced and leads to the formation of a small black slough A negative reaction indicates the presence of sufficient antitoxin to neutralize the toxin

Summary.—The following is a summary of the main points in differential diagnosis

DIAGNOSIS BETWEEN BACILLARY AND AMŒBIC DYSENTERY

BACILLARY DYSENTERY	AMŒBIC DYSENTERY
"Lying down dysentery."	"Walking dysentery"
Acute disease with tendency to epidemic spread	Chronic endemic disease

BACILLARY DYSENTERY	AMŒBIC DYSENTERY
Incubation period short, seven days or even less.	Incubation period in man a lengthy one—at least fourteen to ninety days; may be longer
Onset · Acute	*Onset:* Insidious.
Pyrexia: Common	*Pyrexia:* Rare, unless complicated.
Complications. No hepatitis. Polyarthritis frequent, and occasionally irido-cyclitis	*Complications:* Hepatitis, hepatic amœbiasis, amœbic abscess.
Death due to (a) exhaustion. (b) toxæmia.	*Death due to:* (a) exhaustion. (b) perforation of the bowel. (c) hæmorrhage. (d) liver abscess
Signs Generalized tenderness over abdomen, usually more intense over sigmoid colon.	*Signs:* Local tenderness and infiltration, mostly over sigmoid flexure, transverse colon, and cæcum.
Tenesmus: Very severe.	*Tenesmus:* Usually not present.
Emaciation: Almost invariable.	*Emaciation:* Uncommon.
Pathology: Acute diffuse necrosis of mucous membrane of the large intestine.	*Pathology:* Local lesions confined solely to large intestine, due to characteristic ulcers
Ulcers · When present, situated on free edge of folds of mucous membrane, distributed transversely to long axis of the bowel Ulcers are usually serpiginous with ragged undermined margins, often intercommunicating. Bases consist of granulation tissue, no compensatory hypertrophy of the bowel wall Intervening mucous membrane chronically inflamed	*Ulcers*. "Bouton en chemise"—commence as small abscesses of submucosa, distributed in the long axis of the bowel Ulcers oval, regular, flask-shaped Infection involving all coats of the bowel Bases usually consist of dark necrotic "Dyak hair" sloughs. Ulcers perforate not uncommonly; compensatory hypertrophy of bowel wall Intervening mucous membrane quite healthy.
Stools: Small, numerous Bright red blood, gelatinous, viscid, odourless, resembling red-currant jelly.	*Stools* · Fæces intermingled with blood and mucus "Sago-grain" stool, or sometimes "anchovy-sauce." Copious in amount and usually very offensive.
Reaction: Alkaline	*Reaction*. Acid.
Microscopic: Numerous red cells and polymorphonuclear pus cells Macrophage inflammatory cells (histiocytes). Few bacilli visible.	*Microscopic* Red cells numerous and in "rouleaux." Polymorph cells much damaged, with extruded nuclei. Macrophage cells absent Large numbers of motile bacilli. Active *Entamœba histolytica* with ingested red cells. Charcot-Leyden crystals common

BACILLARY DYSENTERY	AMŒBIC DYSENTERY
Blood examination. No leucocytosis, except in initial stages	*Blood examination:* Moderate leucocytosis.
Serum agglutination Usually serum agglutinates one or other dysentery bacilli	*Serum agglutination* Negative.
Therapeutic test: No reaction to emetine	*Therapeutic test* Almost immediate reaction to emetine
Sigmoidoscopy · Granulation tissue and rigidity of bowel wall Usually no ulcers visible	*Sigmoidoscopy* · Lax and redundant mucous membrane. Small ulcerations with hæmorrhagic margins

Differential diagnosis from the enteric group, food poisoning, cholera, acute ulcerative colitis and other forms of dysentery is dealt with under their respective chapters

CHAPTER IX

THE BACILLARY DYSENTERIES (*continued*): TREATMENT

Bacillary dysentery is a disease which in its early stages appears to be particularly amenable to treatment, so that milder cases recover spontaneously without any particular measures. In the more acute, especially in fulminating cases, prompt and energetic action is necessary, while skill and care in nursing are naturally of importance.

General principles.—The patient should be put to bed, however mild his initial symptoms may appear. He, or she, should be warmly clad and should on no account be permitted to get out of bed to defæcate In addition to general supervision, daily inspection of stools should be made.

Diet.—Special attention must be given to the dietary. Under no circumstances are solids permissible In the more severe forms, which are attended with considerable gastric disturbance, milk is not well tolerated and, as a rule, jellies, weak beef tea, arrowroot, chicken broth, or rice water are preferable. The food should be served slightly warmed and in small quantities, otherwise it is apt to cause increased [illegible]

definitely bland, unirritating, but nourishing.

During convalescence discretion should be exercised. Under no circumstances should patients be rushed through this stage; too rapid introduction of solid food is apt to lead to sudden and profuse attacks of diarrhœa which may result in collapse On the other hand, it is quite unnecessary to keep the patient on a dietary so low in calorie value that he is practically starved.

The following diets have been recommended by J. M. Cowan and H Miller (1918) The chief indication for the change from one diet to the next should be the state of the tongue and the character of the stool Fluids should be given in generous quantities, especially when the diarrhœa is acute During the diarrhœa accompanying convalescence a dry dietary should be instituted

	Diet No. 1	*Diet No* 2
6 a m.	Tea (10 oz).	Tea (can be made with milk)
7 30	Albumin water (6 oz.)	Two beaten-up eggs with tea and milk.

	Diet No 1	Diet No. 2
9 a m	Brand's essence of beef (6 oz)	Barley water.
10 30	Barley water (10 oz)	Benger's
12 noon	Beef tea (10 oz)	Beef tea, custard or rice cooked in water
1 30 p m.	Albumin water (6 oz)	Jelly (2 p m)
3	Jelly	
4 30	Tea (10 oz)	Tea with rusks and biscuits
6	Chicken tea (10 oz)	Chicken tea or Bovril
8	Albumin water (10 oz)	Benger's or arrowroot
10	Bovril (10 oz)	Brand's essence.
12 midnight	Brand's essence (6 oz)	Albumin water
2 a m	Barley water (10 oz)	Bovril
4	Albumin water (10 oz)	Benger's

To either diet citrated or peptonized milk can be added, but it is badly borne when the tongue is coated Chocolate can be added to No 2

No 3 *Diet* Add boiled or poached eggs with junket or milk food (Horlick's or Allenbury's)
No 4 *Diet* Add fresh cream, rice, milk puddings, and toast.
No 5 *Diet* Add fish and bread
No 6 *Diet* Chicken diet, at first without potatoes, vegetables or porridge
No 7 *Diet* Convalescent diet

Moro's apple diet is strongly recommended by German writers (see also p. 457) It consists of apple pulp, up to two pounds a day, with lemons for vitamin C and fluid by the mouth in large quantities

SPECIMEN CONVALESCENT DIET FOR BACILLARY DYSENTERY

Breakfast —
Milk (½ pint)
One egg, lightly boiled
Two breakfast biscuits or rusks with butter

10 a m —
Milk (½ pint)
One biscuit, or rusk

Lunch (1 p m) —
Steamed fish, well pounded, 4 oz
Custard made of one egg and 5 oz milk.
Juice of two oranges in water
A thin slice of dry toast

Tea —
Milk (½ pint)
Three rusks or breakfast biscuits and butter
One lightly boiled egg

Supper —
Scraped beef (1 oz) mixed with Marmite, spread upon a piece of crisp toast and butter
Junket made of ½ pint milk
Juice of two oranges in water

10 p m .—
Milk (½ pint)

Allow 1½ oz. of sugar daily.

Treatment of severe cases.—In enumerating the various methods of treatment, it is proposed to deal first with those cases which are the most severe, for in these irreparable damage is done if the disease is not recognized early and treated efficiently. When once this opportunity is missed, it is no longer possible to restore bowel function.

General measures.—The patient must be put to bed and kept warm with hot-water bottles A warm bed-jacket is advisable, and the abdomen should be protected by flannel binding or by a suitable cholera belt , these measures, besides guarding against chill, afford warmth which is of considerable comfort. The foot of the bed should be raised. The patient should, in fact, be treated on general lines, in

strain, which undoubtedly militates against a favourable outcome. In very collapsed cases incontinence both of urine and of fæces is common, and it is best to pack the buttocks well with carbolized tow or

siderable influence on the bowel.

The mainstay in the treatment of these serious cases nowadays is sulphaguanidine, in conjunction with antidysenteric serum and blood transfusions.

Aperients.—It is a well-established and sane practice to commence treatment by a preliminary purge, in order to clear the large intestine of any remaining fæcal contents. The aperient most suitable for this purpose is castor oil, to which, in order to obviate unnecessary griping, some opium should be added as follows:—

Ol ricin. . . .	½ oz (15 c.c.)
Tinct opii	15 minims (1 c.c)

This should be given preferably last thing at night, and may be repeated

For small children, liquid petroleum, e.g Nujol, in half-drachm doses is probably preferable, and should be given every two hours while the child is awake. T. H Gunewardene (1934) recommends Hydrolax in older children No other purgatives or intestinal antiseptics are required. It is suggested that these preparations act like natural mucus and thus protect the bowel.

to suspect any specific action on the part of the rhubarb, as extracts do not inhibit the growth of the dysentery bacillus

Saline treatment.—Following the preliminary aperient, routine treatment with saline aperients should be begun This is a time-honoured method and one which has received almost universal commendation, especially from Indian physicians and wherever it is necessary to treat bacillary dysentery on a large scale. Most clinicians appear to prefer sodium sulphate to the magnesium salts. It may be given in the following prescription —

Sod sulph	60 gr (4 grm)
Acid sulph. dil.	15 min (1 c c)
Tinct. zingib	5 min (0 3 c c)
Aq menth pip	½ oz (15 c.c.)

It is a well-established rule that a dose of this mixture should be administered every two hours for the first twenty-four, and thereafter every four hours till the stools become fæculent, subsequently it is customary to give it three times a day, but some prefer to give it even more frequently, for instance, every hour for the first forty-eight hours The author prefers the more moderate course

[illegible]

fashioned salines They consider that repeated small doses keep up gentle and continuous peristaltic action, so that the contents of the small intestine are hurried on and toxic absorption is reduced to a minimum The castor-oil-treated series showed a greatly reduced death rate (2 77 per cent as against 8 8 per cent in the saline-treated group) and curtailment of duration of symptoms, while the relapse rate was also considerably smaller

Drugs in bacillary dysentery—*Sulphonamides*—It is pleasant to record that important advances have been made in the treatment of the bacillary dysenteries The present position appears to be that these efficient remedies suffice to cure cases of average severity, [illegible]

Near East.

[illegible]

sodium bicarbonate (to counteract nausea), four times daily for 2–4 days.

The pyrexia was almost immediately reduced and motions became formed in 48 hours These were Flexner and Sonne infections

Bell, in England, had the opportunity of treating a small outbreak of Flexner and Sonne dysentery, with excellent results, by sulphapyridine in

therapeutic activity and the fact that it is poorly absorbed from the intestinal tract ; it thus differs from the so-called intestinal antiseptics

tasteless It appears to be more readily absorbed from the small

assured

Clinical results obtained in a preliminary series of 17 Flexner and

per kilo by mouth Maintenance dose of 0.05 grm. per kilo every four *hours until the number of stools is less than four ; subsequently,* 0 1 grm per kilo every eight hours for at least three days The finely powdered

age from two months to 75 years

The above comprises the medical literature which has appeared

* *i e* the drug is given for 1½ days only.

tenesmus, decrease or disappearance of abdominal symptoms, fall in temperature and pulse rate, together with a remarkable reduction in the number of stools As a rule, within 5–6 days the bowels act once or twice daily, and blood disappears rapidly from the fæces In the acute cases [illegible]

doses suggested are 18 grm in the first 24 hours, administered in 6 grm doses three times a day after meals, subsequently 3 grm three times a day for five days

The earlier that treatment with sulphaguanidine is commenced, the less extensive is the damage to the colon and the more rapid the recovery The most dramatic cures were found in acute cases treated within 24–36 hours of the onset In the fatal cases, where failure appeared to have occurred, some complicating factor was proved to be present

The action of sulphaguanidine is either bacteriostatic or bactericidal and leads to immediate decrease in toxin production, but appears to have no effect on dysentery exotoxin absorbed into the blood These writers consider that the best results will be obtained by combining sulphaguanidine and Shiga antitoxin (antidysenteric serum) in fulminating Shiga dysentery in which it is imperative that circulating toxin should be rapidly neutralized No severe toxic manifestations were noted, exceptionally there was a transient papular eruption. The toxic nephrosis (toxæmic nephritis), which has been found not infrequently complicating bacillary dysentery, has no relation to administration of the drug It is said to be less efficacious in Sonne infections, but a new compound of the same series, sulphamethazine, is reported more satisfactory

D F W [illegible]

was to be avoided

Medicinal charcoal, a tablespoonful three times daily, is useful as an intestinal disinfectant, and carbo medicinalis "Merck" is strongly recommended by Weiss (1927)

Isogel, a granular preparation of agar produced by Allen and Hanbury,

given in teaspoonful doses, is useful in solidifying the stools and checking the diarrhœa

The author is strongly opposed to the use of *opium* as a routine measure in the treatment of dysentery, and preparations of opium, morphia, laudanum, and chlorodyne, however comforting, must not

should be confined to procuring rest and sleep and to enabling a patient to withstand the fatigue and trials of a long journey, as, for instance, evacuation from a field ambulance in war time. Morphia should be given preferably by the hypodermic route, but in doses no larger than ¼ gr (0 016 grm).

had taken place

In Germany and Austria the exhibition of *kaolin* with the addition of animal charcoal, in doses of three tablespoonfuls of each, is much used and is well spoken of It is probably better to give the preparations known as colloidal kaolin or Kaylenol

Some patients do not tolerate saline aperients well, and in these *calomel* (½ gr every hour for twelve hours on three consecutive days) is used

Intestinal disinfectants.—These have been much used in the

the mass treatment of bacillary dysentery. In fact, they consider that serious

Preparation of antidysenteric serum.—In the British Pharmacopœia for 1932 it is laid down that the potency of antidysenteric

Storage.—Antidysenteric serum (Shiga) should be kept at as low a temperature above its freezing point as possible. It should be stored in glass phials, preferably not in bottles with rubber caps, as these, especially in the tropics, are very apt to be contaminated. In the tropics, too, the serum must be kept on ice, because there is no doubt that continuous heat causes a considerable diminution in antigenic power

Principles underlying serum-therapy.— The first serious attempts to produce an efficient antitoxin in bacillary dysentery were made by C Todd in 1904, in London, and L. Rosenthal (1903, 1904) in Moscow They showed, quite independently of one another, that the soluble toxin contained in cultures of Shiga's bacillus was capable on injection into animals

recently dysentery anatoxin has been used for its production (Dumas and others, 1926).

The titration of this serum is best carried out by intravenous inoculation in mice.

antidysenteric sera lies in the fact that such sera contain but small amounts of efficient Shiga-immune bodies It is apparently much easier to produce an efficient anti-Flexner serum but, as the most acute cases of bacillary

Serum-therapy.—No consensus of opinion can be obtained on which class of case should receive anti-serum treatment. In the author's opinion care should be exercised in the selection of cases and the

selected, it is necessary to observe strict aseptic precautions. In every case the serum should be heated to body-temperature by being placed in a vessel of water at a temperature of 110° F. (43 3° C) for fifteen minutes

W E Waller (1919), in Mesopotamia, and B. G. Klein (1919), in France, treated over 1,800 cases by subcutaneous injections of Lister Institute polyvalent serum Large amounts in doses of 120–140 c c. were found most beneficial. This amount of serum can be given in three injections at eight-hour intervals From the seventh day of the disease onwards the serum has less effect; by this time, usually, either

given
e the

glutei muscles or the adductor group in the thigh, where the tissues can accommodate large quantities of fluid Intravenous injection into the median basilic vein in doses of 60–80 c c has been employed in very acute or fulminating cases In collapsed patients it may well be diluted with 100–200 c c. of saline solution containing 5 per cent. glucose

P. J Lantin (1921) reported favourably on a method, practised in the

solution, with fifteen drops of laudanum. A high enema of serum, 30-80 c c, should be given half an hour later Lantin believes that a combined method of intramuscular and rectal injection in acute cases offers the best chance of success. W. Willcox inclined towards this method as avoiding the dangers of serum reactions.

Monovalent anti-Shiga serum.—Much of our information on the therapeutic effects of anti-dysenteric serum was derived from experiences in the War of 1914–1918, when a polyvalent serum was employed. Since that time, however, great improvements in the preparation, refining and concentration, especially of anti-Shiga serum, have been effected As issued to the Army in the present emergency it contains 50,000 international units in a volume of less than 10 c c. Between

it is fleeting and temporary

Practical results.—The treatment of bacillary dysentery with antidysenteric serum has been practised now for over thirty years.

[illegible]

December, 1910

Date	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3
Time	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E	M E

Chart 2.—Bacillary dysentery (Shiga) treated by injection of antidysentery serum.

patient by repeated daily doses The injection of the serum in this way is followed by a rapid decrease in the toxæmia H W Joseph and W. C [illegible]

[illegible]

instase In very sick children the intramuscular route is contra-indicated on account of the pain elicited at the site of the injection M De Biehler (1922) thinks that serum rash, which is common in children, can be avoided by giving calcium chloride

Treatment by sensitized dysentery vaccine.—*Boehncke's Dysbalta* (see p. 113) or a polyvalent sensitized dysentery vaccine, has been employed extensively in Germany, especially in the treatment of children. Schittenhelm (1918) and Schelenz (1918) reported favourably on this combined

specific treatment in both acute and chronic cases. Gross (1918) considers that in the very acute case, where the body is incapable of reaction, the vaccine is

at 37° C for several hours, washing in sterile normal saline and
56° C for one hour Doses from 50–200 million sensitized bacilli can be used.

Treatment of pregnant women.—In pregnancy, bacillary dysentery should be regarded as a serious event owing to the likelihood of abortion The use of aperient salines should be carefully regulated for the same reason, and it is advisable to give half doses.

Treatment by specific bacteriophage. — F. d'Herelle has claimed that favourable results have been obtained in suitable cases by the administration of bacteriophage, but the results so far are not, to the critical eye, very impressive.

A Compton (1929) prepared a therapeutic "phage" by putting up a mixture of four phage strains against sixteen-hour broth cultures of two Shiga,

Treatment of special symptoms. *Mouth*—The mouth must be kept clean by means of special mouth-washes (e g , Lavoris), and by swabbing the tongue and the gums frequently with glycerin and borax.

Abdominal pain is best relieved by the application of hot-water bottles, turpentine stupes, or the Japanese hot-box, i.e., a tin box containing slowly-burning charcoal (known under the name of Istra), three or four of which should be sewn in flannel and placed upon the abdomen.

Tenesmus and dysuria are best relieved by hypodermic injections of morphia, or by the insertion of cocaine and morphia suppositories Hot douches into the rectum, slowly administered by means of a tube and funnel, have also been found to be of value The rectum can be lavaged with warm saline solution, boracic solution (1 dr (3 8 grm.) to 1 pint of water) or 0 5-per-cent tannic acid The temperature of the douches should be about 101° F. (40° C)

[illegible]

water bottles and stimulated with brandy by the mouth or by enema, [illegible]

have advocated amidopyrine in large doses, and also cocaine

For flatulence and meteorism, charcoal biscuits, granular charcoal or charkaolin are useful

Toxaemia —B Gantenberg and others in Poland (1939) have [illegible]

intravenous salines Under war conditions plasma or dried reconstituted plasma appear to be equally efficacious

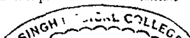
H Otto (1940) found that subcutaneous injections of adrenalin were beneficial

Chronic Bacillary Dysentery

The specific organisms which caused the initial trouble, the dysentery bacilli, play little part in the terminal stages of this disease, so that the destruction of the mucous membrane and its replacement by granular tissue has to be regarded as the aftermath of their activities The problem is a mechanical one the efforts of the practitioner should be directed towards diverting the fæcal stream as much as possible from the large intestine, and putting it in a state of almost complete rest so that healing may have a chance to take place

The line of treatment here advocated may be divided into three headings dietetic measures, intestinal medication, and operative interference

Dietetic measures.—The diet should be carefully regulated, monotony being avoided The author considers it a mistake to starve the patient; he should be provided with as much simple and easily assimilable food as it is possibl[illegible] o tolerate The main object



should be to stimulate the recuperative powers of the body so as to aid in regeneration of the intestinal mucous membrane. Oils and fats are

J. P. Lockhart-Mummery and others in the treatment of ulcerative colitis and other chronic diseases of the colon.

and it should be tried as a preliminary measure.

Intestinal medication.—The bowels should be cleared out by a small dose of castor oil, followed by a large enema of hot water, 2–3 pints (1,700 c c) to which 2 drachms (7 grm) of sodium bicarbonate have been added This enema is intended to remove the mucus and débris which has accumulated on the surface of the bowel, and as such it appears to be useful

The other medicated fluids that are injected are intended to exert some healing action upon the bowel surface The most efficient of these with which the author is acquainted is *Eusol*, but unless this is given highly diluted at first, it is apt to be too irritating and cannot be tolerated The author commences treatment by the injection of a half pint of a dilution of 1 part of eusol (Budge's eusol is preferred) to 9 parts of water. The enema should be retained by the patient as long as possible, usually from five minutes to three-quarters of an hour. If this is satisfactory, the subsequent daily injections should be in increasing strength of eusol; for instance, on the second day 2 parts of eusol to 8 parts of water, and so on until half-and-half solution is obtained. This produces some pain in the lower bowel, due to its stimulating action

Technique.—The solution should be run slowly into the rectum by a rubber catheter, the patient recumbent on his left side. The catheter should be made of stout rubber and provided with a round terminal opening. Attempts to pass it higher up into the rectum usually tend to create a kink.

When the patient senses that the solution has entered the sigmoid the knee-elbow position should be adopted for five minutes and then he should lie on his right side

This treatment may be persisted in for 3-4 weeks, but if too exhausting, injections should be given on alternate days

H J Smyly (1930) reports good results from intestinal lavage with Dakin's (weaker) hypochlorite solution (Solution Dakin K C H.) A 20-per-cent.

solution can easily be tolerated and the strength is increased each day as rapidly as the patient can bear it. Some cases are cured with solutions not [illegible]

healed and signs of acute inflammation have subsided

For rectal irrigation through a colostomy the following apparatus is required :—

A cylindrical glass funnel, 1½ in in diameter, and graduated to hold 10 oz of fluid The lower part should be provided with a constriction so as to [illegible]

A bulbous glass connecting tube for joining to the rectal tube

A narrow tube necessary for securing all junctions tightly

Rubber gloves for the operator's hands, and a plentiful supply of vaseline.

MEDICAMENTS FOR COLONIC IRRIGATION*

Silver salts.—*Albargin* (silver gelatose) 20 gr to 20 oz (1 pint) of normal saline, a 0 25 per cent solution *Argyrol* (a vegetable protein compound of silver) 40 gr to 20 oz (1 pint) of normal saline, a 0 5-per cent solution [illegible]

Note that all silver compounds are soluble only in cold water

H J Smyly recommends the use of these silver salts, even silver nitrate, [illegible]

precipitate the silver [illegible]

enemata.

Bile extract (Fel bovinum purificatum, 20 gr to 2 oz of water) added to the enema is said to increase the peristaltic action of the colon and so to reduce flatulence

Bismuth subgallate (dermatol) can also be given by the mouth in doses of 30–90 gr daily As a retention enema in a 5-per-cent solution

* See also Chapter XXIV

should be to stimulate the recuperative powers of the body so as to aid in regeneration of the intestinal mucous membrane. Oils and fats are particularly useful, because they tend to lubricate the raw surface of the bowel—thus helping to promote healing—and also, possibly, because of their vitamin content. In principle this is the policy advocated by J. P Lockhart-Mummery and others in the treatment of ulcerative colitis and other chronic diseases of the colon

Intestinal medication.—The bowels should be cleared out by a small dose of castor oil, followed by a large enema of hot water, 2–3 pints (1,700 c c) to which 2 drachms (7 grm.) of sodium bicarbonate have been added This enema is intended to remove the mucus and débris which has accumulated on the surface of the bowel, and as such it appears to be useful

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H. J. Smyly (1930) reports good results from intestinal lavage with Dakin's (weaker) hypochlorite solution (Solution Dakin K.C.H) A 20 per-cent.

addition of eusol is soothing and effective, and may be followed by injection of tannic acid

Solutions of tannic acid for the healing of ulceration may be made up as follows.—

Tannin .	5 grm
Tinct opii.	1 c c
Arrowroot	15 grm
Water to	1 litre

Half a litre to be injected slowly.

Solution for tenesmus and sphincteric cramp.—A starch and opium enema is very useful on occasions, but in case of failure the following is recommended (W K Russell, 1932) —

Calc chlorid	10 grm (154 gr)
Mag chlorid.	5 grm (77 gr)
Sod bicarb	5 grm (77 gr)
Omnopon	0 04 grm (⅗ gr)
Tinct bellad	3 0 c c (51 mins)
Water to	20 litres (4½ gallons)

A pint or more to be used at a time.

Ispaghul —For centuries it has been the custom in India to treat cases of chronic diarrhœa and dysentery empirically with the seeds of Ispaghul (*Plantago ovata*)

Undoubtedly when eaten in their natural state these boat-shaped

bowel, should be employed, unless it causes increase of pain and peristalsis

Sulphaguanidine —The reports on this sulphonamide so far received seem to indicate that it is of distinct value in chronic bacillary dysentery (see p 94)

Nipectin —American workers have discovered in pectine and pectinates, the metal derivatives of pectin, a specific substance for the treatment of bacillary dysenteries and allied conditions Pectin is the intracellular cement of the cell-wall tissues in fruit and succulent vegetables, especially in citrus fruits, possibly its presence in apples explains the value of Moro's apple dietary The commercial product is

suspended in 8 oz. of olive oil, for ten days consecutively, it has a soothing and healing effect in ulcerated cases. Can be used in a strength as high as 10 per cent

Bolus alba (kaolin, 3 drachms to water, 1 oz , used in suspension) can be given as a retention enema.

[illegible]

Glucose may be given as an enema in the strength of glucose 1 oz to 1 pint of normal saline

Ichthyol (ammonium ichthosulphonate) in 0 5–1 0-per-cent. solution The ichthyol should first be dissolved in a few drops of glycerin, and the *requisite amount of water added. Two pints of this solution should be injected* slowly into the bowel and retained as long as possible.

Kamillosan, a preparation of chamomile flowers (*Matricaria chamomilla*) is employed in a strength of 2 drachms to 1 pint of warm water. It has an anodyne and antispasmodic effect (Spicer and Co , Watford, Herts)

[illegible]

is advisable two hours beforehand

Mercurochrome *should be given dissolved in normal saline in a 1-per-*cent solution (4 gr to 1 oz) A few drops of dilute acetic acid may be added. It is used as an intestinal disinfectant in a 1- to 2-pint enema.

Milton, a disinfectant and deodorizer (sodium hypochlorite, sodium chloride and small quantities of chlorate, sulphate and carbonate and calcium chloride) as an enema in strength of 1 fl. drachm to 2 pints of warm water

Potassium permanganate as an oxidizing agent for destroying intestinal bacteria and their products, in a strength of 1 gr to 1½ pints, may be given with safety twice daily

• **Slippery elm** (*Ulmus fulva*) is used as a demulcent. Two sheets of the bark, 12 in by 8 in , are cut into fine shreds and immersed in 8 pints of water *The liquid is then brought slowly to the boil and allowed to simmer* for two hours and strained

Saccharated alkaline saline solution (J. G Willmore) is prepared as follows —

Kitchen salt (NaCl)	1 large tablespoonful
Sod. bicarb	1 " "
White sugar	2 " "
Warm water	2 quarts

Two pints can be tolerated

Tannic acid (40–60 gr to 1 pint of warm water) is most useful, on account of its astringent effect, in cases where there is much bleeding In cases of hæmorrhage, hypertonic saline solution (NaCl 120 gr. to 1 pint) with the

impossible to close the cæcostomy opening on account of the destructive process in the large intestine, and he continues to pass blood and mucus *per rectum* daily.

In valvular cæcostomy œdema and thickening of the cæcal walls may render the introduction of a Paul's tube difficult so that provision should



Fig. 15 —Tampon tube.

after insertion the tube tends to become loose, when the liquid and
This discharge is
rotected by liberal
my belt should be

Unfortunately, complete drainage of fæcal material is not obtained even when the cæcum is opened in this manner, for peristaltic movements continue to drive a certain amount of the fæces along the colon In order to combat this A L Gregg (1926) devised a tampon tube (Fig 15) consisting of a soft rubber bulb which, soldered round the rectal tube, can be inflated With the bulb, B, deflated, the tube, A,

The lumen of the ascending colon is thereby blocked, so that the upward passage of fæcal material becomes impossible At the same time, the central tube, A, permits colonic lavage, reflux being prevented by

obtained from the rind of citrus fruits and from apple "pomace" (in the manufacture of cider). When mixed with acid, sugar and water, it forms a jelly and with metals assumes a colloidal form. Silver and nickel pectinates appears to possess definite bactericidal properties and the latter, moreover, functions as a catalyst and assists in the absorption of vitamins.

Nickel-pectin compound is dispensed by Eli Lilly & Co. as "Nipectin"; when mixed with an equal volume of icewater it has a faintly acid taste and, *in order to prevent the formation of gummy masses, it should be*

fæcal

anti-hæmorrhagic properties.

Surgical treatment.—The author has no hesitation in advising early surgical interference whenever medical measures fail. The indications for operation should be based upon signs of toxic absorption, intestinal hæmorrhage, and sigmoidoscopic appearances of the bowel indicating grave destruction of the mucous membrane. It is not *justifiable to postpone operation until the patient is almost in extremis.* Should he continue to lose weight with medicated enemata it is an

fæcal drainage.

Appendicostomy and valvular cæcostomy (*see* p. 458).—*These operations may be considered together, as in the main their* actions are identical, and may be illustrated by the following:—

An ex-soldier of thirty was operated upon in 1924 after suffering continuously for three years with chronic bacillary dysentery to which he nearly succumbed

wound after withdrawal of the tampon tube, in order to hinder fæcal exit through the wound

Ileostomy (*see also* p 460) —Ileostomy in continuity—unless [illegible]

irritation

TREATMENT OF COMPLICATIONS

Arthritis —Dysenteric arthritis with effusion is best treated by placing the limb on a back splint, by application of Scott's dressing, by radiant-heat treatment for half an hour daily, and later, when absorption has occurred, by massage When the joint cavity is greatly distended with fluid, aspiration generally relieves the pressure temporarily In addition to the local treatment of the joint, detailed attention to the bowel is necessary. Therefore lavage with eusol or with sodium bicarbonate should go hand in hand with the local measures B Hughes and H S Banks (1920) recommend early aspiration of the joint and injections of 5 c c of ether into the joint cavity A general anæsthetic is required Under modern conditions sulphaguanidine treatment is indicated

Eye symptoms —Conjunctivitis should be treated by local applications of boracic acid; and irido-cyclitis by instillation of atropine drops (1 grain to 1 oz of water) combined with an eye shade Attention must be devoted to bowel treatment

Parotitis may become suppurative, and should therefore be taken seriously. It should be treated by fomentations and strict attention to the hygiene of the mouth

Malaria.—The complication of malaria should never be overlooked, especially when it is a primary infection with the subtertian parasite In this case primary attention must be paid to the malaria aspect An intramuscular injection of quinine bi-hydrochloride 12 grains (0 76 gramme) should be given, reinforced by atebrin (0 1 gramme) three times daily for at least ten days (*See also* under Malarial Dysentery, p 268)

Prognosis.—The prognosis in bacillary dysentery depends very much upon the intensity of the particular epidemic and on the age and physical condition of the patient It is not possible to lay down definite rules, as the data upon which one can base an estimate are somewhat insecure, but prognosis is by no means good in small children The disease is often fatal, also, to young adults, especially when they hail from countries such as Australia and New Zealand (as during the 1914-18 War), where bacillary dysentery is unknown or very rare

In cases with persistent vomiting or with collapse, the prognosis is not good, while a persistent hiccough may be regarded as being, almost invariably, a fatal sign. The outlook is not good, also, in those cases

be expected to improve, but such an improvement does not, unfortunately, do away with the attendant's anxieties, for the difficult problem of when to close the wound has to be decided. Patients naturally object to being left with a permanent colostomy.

After some months of disuse a severely ulcerated bowel may become so stenosed that any attempt to close it is doomed to failure on account of obstruction This condition has been observed in three

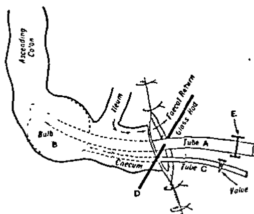


Fig. 16.—Diagram showing tampon tube in position.

instances, and it demonstrates the need for constant attention and supervision Should evidence of stenosis be observed, the patient must be warned that closure of his wound has become impossible It is on this

be observed, it can safely be removed and an anastomosis performed.

The following are indications for closure :—

disease by prophylactic vaccination, but so far they have not, apparently, been attended by great success. Attempts at passive immunization by injection of antidysenteric serum appear to afford a protection which lasts from four to six weeks

Prophylaxis

Personal prophylaxis consists of careful attention to personal hygiene, of care in the conservation and preservation of food in the tropics, and, especially, of taking precautions against contamination of articles on the table or in the kitchen

Stools which are required for bacteriological purposes should be dispatched to the laboratory in sterile receptacles with well-fitting lids. Disinfection of *fæces* is necessary, and those passed by dysenteric patients should be protected against the entry of flies and sterilized, as far as possible, by pouring over them crude carbolic or Jeyes' fluid

Water must be sterilized, it should be boiled before use and efficiently protected against subsequent contamination. Appropriate measures should be taken with ice, fruit and vegetables in localities where bacillary dysentery exists.

Milk also can be infective, and becomes contaminated through the vessel in which it is stored, by addition of infected water, or by fæces of infected flies. In tropical and subtropical climates all milk should be pasteurized or boiled before use and then properly protected against flies, dust, and other contamination

The danger from *flies* has already been discussed, and it is hardly necessary to draw further attention to the murder-bearing flight of these insects from latrine to larder. The common breeding-grounds of the house-fly—the manure heap, the dustbin, and the latrine (especially the dry-closet)—demand especial attention

Nursing.—Bacillary dysentery cases are infectious, and to no one are they more so than to the nurses who tend them. They must be tended, therefore, in wards set apart for this purpose and nurses must be warned of the danger they run and should be trained in prevention of this disease.

medical care, unless he is able to take ordinary food without intestinal upset, and it is questionable whether the usual three negative bacteriological examinations of fæces are all-sufficient in this respect. Therefore

which, from the start, pass stools containing a large amount of dark altered blood, or greenish-coloured sloughs.

Patients suffering from valvular disease of the heart do not bear the physical strain of bacillary dysentery well, nor do women in advanced stages of pregnancy. As has been mentioned, primary attacks of subtertian malaria in bacillary dysentery are a dangerous combination, so also is broncho-pneumonia, lobar pneumonia, beri-beri, scurvy, Bright's disease, tuberculosis, or other grave constitutional disturbance.

C. Froemsdorff (1923) quotes figures obtained from reliable German sources extending over the period 1916–20. In 1916, in a series of 12 cases, the death rate was 8.33 per cent.; in 1917, in 109 cases, it was 29 35 per cent.; in 1918, in 277 cases, 14.07 per cent.; in 1919, in 68 cases, 8 82 *per cent.*; *and in* 1920, *in* 59 *cases*, 13 55 per cent In the whole series of 525 cases, 415 recovered (79.04 per cent), 22 were improved (4 19 per cent.), and 86 died (16.38 per cent), and in 2 cases (0.38 per cent) the condition *remained unchanged. The death rate was high, especially in elderly* patients and in those who were greatly debilitated as the result of war privations. This is by no means an exceptional series, for in the industrial districts of Westphalia the death rate from this cause stood at *10 per cent. Out of a series of 210 cases, whose subsequent career* could be traced over a period of six years, in three, or 1.43 per cent., the disease became chronic The figures from British sources during the 1914-18 War do not convey much information on this *subject, and have been dealt with by the author in the Official History* of the War.

Natural and acquired immunity.—It is difficult to write about immunity to bacillary dysentery because of the paucity of accurate *observations, but the following generalized statements may be made.*

There appears to be no *natural immunity* to bacillary dysentery; the

...appear to be more susceptible than are residents.

account that immunity may be produced towards one bacillus, while at the same time a greater susceptibility to other dysentery organisms may develop. Ingestion of a sub-infectious dose may convey the immunity to those who have shown no external evidence of the disease.

Attempts have been made actively to immunize man against the

hydrogen peroxide in place of eusol They recommended a vaccine containing 200 million Shiga bacilli per c c inactivated at 58–60° C for one hour L Dudgeon (1919) reported that his experience with eusol treated Shiga vaccines was unsatisfactory

The Japanese first employed a sero-vaccine Graeme Gibson conducted a research on this subject and found that, although the local reactions were mild, no considerable production of antibody took place. It was concluded [illegible]

[illegible]

favourable, it was largely used in France during the later stages of the 1914 18 War

In Macedonia, in 1918, Gibson's sero vaccine was tried with the following results (L Dudgeon, 1919) —

		Cases of Dysentery
Non-inoculated,	2,096	67
Inoculated,	1,147	14

The results show that a considerable measure of protection had been obtained, and that this protection remained for at least a year

A somewhat similar method was applied in Germany and Austria ("Boehncke's *Dysbakta*") Boehncke and Elkeles (1918) reported that [illegible]

[illegible] H M Perry and C J Coppinger found that vaccines of Shiga's bacillus prepared from anaërobic cultures were much less toxic than those prepared from cultures grown in an aerobic manner They therefore advocated a mixed vaccine prepared from anaerobically grown Shiga bacilli and [illegible]

[illegible]

bacillary dysentery took place He thinks that there is some evidence that inoculation of contacts and of all persons liable to infection cuts short spread of this disease

[illegible]

those with positive skin reactions cannot do so

L Otten and L Kirschner (1925) found that a formolized heated suspension

which appears particularly effective in the carrier state, should greatly simplify this problem in the future It has been emphasized that this drug acts most effectively when the fæces are fluid, so that it may be necessary to combine it with routine aperients.

Susceptibility.—In considering prophylaxis against bacillary [illegible]

(3) Native labourers and paupers or vagrants, mortality 25 per cent.

[illegible]

is a healthy intestinal mucous membrane.

Prophylactic vaccination.—The question whether one attack of [illegible] dysentery affords absolute protection against future ones is a

subject is now very profuse, but it is in such a state of confusion that it almost defies analysis Reference may be made, however, to a few of the more important papers

C. Nicolle and E Conseil (1922) have criticized Besredka's results on the above-mentioned lines

In 1925, C Seyfarth tested this method among the Greek refugees in camp at Phaleran, Greece, and claimed that the onset of dysentery was prevented in 340 refugees vaccinated by the mouth A Gauthier (1924) reported 30,000 antidysenteric vaccinations by mouth to refugees in Greece and Macedonia It is claimed that no cases of dysentery occurred among those so treated Liquid polyvalent vaccines containing 35,000 million bacilli per c c were given one hour before food

In 1927, M N Fulton and G P Berry tried oral vaccination against Flexner's bacillus on children under two years of age in the United States [illegible]

E. Vaz (1929) and E de Araujo and O Torres declared themselves warm supporters of the oral administration of dysentery vaccine, both for prophylactic and curative purposes, and stressed the importance of thus immunizing a backward and insanitary population

[illegible]

noted as the result of the administration [illegible]

living dysentery vaccine

of dysentery bacilli was preferable to anatoxin (formolized heated dysentery toxin) and caused far less marked local reaction. They claim that these formolized suspensions produce immunity

M Sardjito (1926) employed a method of immunization by a lysate (bacteriophage) of Shiga-Kruse bacilli, treated with formol, 1 c c. of the formol-treated lysate, after neutralization with caustic soda, being injected subcutaneously. No after-effects are said to be noticeable.

W. Troitzki and his colleagues (1940) have shown that ultra-violet rays on *B. dysenteriæ* remove toxicity. Vaccines made from cultures so treated will [illegible]

[illegible]

and mice showed that it is possible to find a dose of suitable composition and of low toxicity which protects animals against subsequent injection of two lethal doses of combined toxins. The efficacy of this method consists in the appearance of antitoxin in the blood.

Oral vaccines.—For some time past Besredka has been studying what he terms local immunity in infectious disease. From his work and that of others on local immunity produced in the skin of guinea-pigs against anthrax and [illegible]

The Protozoal Dysenteries

CHAPTER X

AMŒBIASIS: EPIDEMIOLOGY AND GEOGRAPHICAL DISTRIBUTION

Synonyms.—The term amœbiasis includes tropical, endemic, or amœbic dysentery, amœbic enteritis, amœbic colitis; and primary or intestinal amœbiasis

The secondary manifestations of amœbiasis include hepatic amœbiasis (amœbic hepatitis), amœbic abscess of liver (tropical hepatic abscess), lung (pulmonary amœbiasis), brain, spleen and epididymis Amœbic ulceration of the skin may also be included

French Dysenterie amibienne, *Italian* Dissenteria amebica, *German* Amöbenruhr

French Abscès hépatique amibien, *Italian* Ascesso epatico, *German* Tropischer leberabszess

French Abscès cérébral, *Italian* Ascesso cerebrale, *German* Gehirn abszess.

Definition.—Amœbiasis denotes infection with protozoal organisms

Preliminary.—Certain considerations must necessarily preface a systematic description of amœbiasis Difficulty arises from the fact that amœbic dysentery is not, probably, the most common expression of amœbiasis The normal habitat of *Entamœba histolytica* is the mucous membrane and submucous layers, where it feeds upon the cells, being enabled to rend or dissolve them by means of proteolytic ferments. In this manner the amœbæ live and multiply at the expense of the tissues of their host who is, in ordinary circumstances, quite capable of compensating for the ravages of these organisms without detriment to health This state of equilibrium is probably the commonest condition met with in amœbiasis in the tropics and gives rise to the "carrier" or "cyst-passer" state Such a condition causes no outward signs of ill-health, and can be verified solely by

they serve the double purpose of ablution and defæcation. In the tropics, also, rivers are commonly contaminated by natives, and so are

Epidemiology

In contrast to bacillary dysenteries, amœbiasis shows a somewhat localized distribution; it is therefore unlikely that amœbic dysentery, liver abscess, or other complications can commonly break out in epidemic form It can be concluded, generally speaking, that epidemics of dysentery are bacillary in origin, while sporadic cases are due to amœbiasis The so-called "epidemics" of amœbic dysentery which have been reported, especially during the 1914-18 War, should be regarded with suspicion as indicating that there was confusion between amœbic and other forms of dysentery.

When many cases of amœbic dysentery occur simultaneously in a locality, it indicates that patients have simultaneously contracted their infection from a common source, and further indicates that there must be, in that area, a larger number of carriers of *E histolytica* cysts than cases of dysentery To make this point quite clear, it must once more be emphasized that the sufferer from acute amœbic dysentery is unable to transmit the disease and is therefore non-infective to others The Chicago "epidemic" to be described later may constitute an exception (p 122)

Transmission by flies.—J G Thomson and D. Thomson (1916) were the first to note that house-flies (*M. domestica*) could transport cysts and pass them unchanged in the dejecta In the same year P C Flu concluded, from a study of the mouth parts of the house-fly and bluebottle (*C erythrocephala*), that cysts of *E histolytica* could survive in their intestines In 1917 C M Wenyon and F W O'Connor were able to ascertain that viable *E histolytica* cysts could be demonstrated in fly excrement sixteen hours after a feed, and moreover, that cresol 1 40 was most effective as a disinfectant for cysts, preventing their spread by insects P A Buxton (1920), in extensive observations on flies in Iraq, dissected 1,027, and of these 68 per cent contained "apparent" fæces, and 0 8 per cent cysts of *E histolytica*

From this it can be concluded that, under tropical and sub-tropical conditions, house-flies may act as disseminators of amœbic dysentery.

Transmission by water.—H. M. Woodcock (1918), as a result of

discovery of encysted forms of amœbæ in the stools. Such a carrier cannot, however, be described as being perfectly normal, because some lesion or abrasion of the intestinal canal must exist, and, under certain circumstances, the nature of which is not fully understood, he may develop amœbic dysentery or—it may be—liver abscess.

The genesis of amœbic dysentery appears to be that the amœbæ, under certain conditions, destroy the tissues at a more rapid rate than nature can repair them All degrees of ulceration of the intestine may therefore result, from a minimal effect producing a transient illness or diarrhœa, to intense ulceration of the bowel, with destruction of the greater part of the mucous membrane and passage of blood and mucus, containing numbers of active amœbæ. This ulcerative colitis is known as *amœbic dysentery*; but blood and mucus may not be

amœbiasis. When amœbic invasion is arrested in the liver, *amœbic hepatitis* is produced, and this process may result in *amœbic abscess* of the liver. These parasites may produce abscesses in other organs—e g., in the lung, or, very rarely, in the brain, spleen and epididymis.

As compared with bacillary infections, amœbic dysentery is a comparatively mild disorder, causing less serious illness and fewer fatalities, and is less infective and not so readily communicable. It would be an error, however, to infer that amœbiasis may not be severe or even

eaten raw It cannot therefore be sufficiently emphasized that no raw vegetables or unpeeled fruit should be eaten in the tropics.

J Andrews has demonstrated that amœbic cysts can survive fæcal contamination of the fingers, and remain viable for at least forty-five minutes, but are difficult to detect under the nails of adequately washed hands

B. K. Spector and F. Buky (1934) have shown, by using the eosin test as an indicator, that cysts of *E. histolytica* perish rapidly in dry fæces at room temperature.

It thus appears improbable that amœbiasis can spread in those countries where sanitation is good, as in most European countries, and where there are no native servants, who may constitute a perennial source of infection

It is difficult at present to assert which of the various methods indicated is of the greatest importance in the transference of amœbic infection. This can be solved by more extensive work on these lines

Lowered resistance of the patient to infection is undoubtedly also a factor, and this, together with defective sanitation, is probably chiefly responsible for the high incidence of amœbiasis in tropical and sub-tropical countries.

be due in part to the care that is usually exercised by their parents in guarding them against sources of infection. The author has never seen a case of intestinal amœbiasis in a European child of under five It is essential that amœbic dysentery in children should be diagnosed with great care, mainly because emetine, if used indiscriminately, may cause severe toxic manifestations.

TABLE VIII

AGE INCIDENCE

Age	Amœbic Dysentery (257 cases)	Liver Abscess (169 cases)	Total (426 cases)
Below 10	0 9	0 0	0 6
11-20	12 5	6 1	9 6
21-30	32 8	37 0	33 3
31-40	28 5	39 8	32 6
41-50	17 4	9 7	15 6
51-60	4 8	6 0	5 6
61-70	2 7	0 7	2 1
71-80	0 4	0 7	0 6

water was no longer adequately controlled or sterilized, the inference being that troops were being infected from fæcally-contaminated well-water.

brought from Lisbon which was stored in large tanks liable to contamination A similar instance has been reported by R. Hegner (1934) in Guatemala

The epidemic of amœbic dysentery in Chicago during the summer and autumn of 1933 (June 1st to December 31st) was the first recognized water-borne outbreak and the best known extensive epidemic of this disease in a civilian population.

During the epidemic period, which coincided with a Century of Progress Exhibition, there were approximately 8,500,000 out-of-town visitors to Chicago, resulting in unusual congestion. Only one focus of infection was discovered, namely, two hotels which were served, in part, with a common water supply. During this period a total of 1,409 cases was brought to light, even with incomplete reporting. Approximately 75 per cent had had contact with one or both of the hotels, with the result that amœbic dysentery contracted from this source was reported subsequently from 400 cities in America.

There was a particularly high incidence late in June, during the latter half of August, and early in October Of those exposed during the peak periods some 5 per cent. acquired the disease. Generally speaking, the more prolonged the exposures at these hotels the greater the hazard of infection The excessively high rate of clinical dysentery was in strong contrast to the results of previous observations on this disease and may be explained

overloaded to an unusual degree during the period of the epidemic, owing to excessive rainfall and unusual pressure on accommodation. The source of pollution of the water supply, which was common to both, was found to be a rotting wooden plug in an overhead sewer which permitted leakage into the drinking-water tank below.

Transmission by human excreta.—There remains another possibility—that cysts are ingested with green vegetables and raw fruit in those areas, so frequent in the Near East and the tropics,

and H. E. Meleney (1931), and by E. L. Bishop and W. S. Leathers show that the height of the incidence curve for *E. histolytica* occurs between 26 and 30 years but that after 35 there is a rapid decline in the incidence.

Sex incidence.—With equal chances of infection, it is probably true that women are as frequently infected as men, but European males preponderate in most parts of the tropics, consequently a much larger number is infected. Moreover, owing to their occupation, men are more exposed. The author's statistics in London show that the proportion of males to females was four to one, the latter are less susceptible to liver abscess, the author having encountered only six cases, which suggests that this infrequency may be more than accidental.

Race incidence.—All races appear to be liable to infection by *E. histolytica*, though it is undoubtedly true that Europeans in the tropics as a rule suffer from amœbic dysentery more frequently and [illegible]

Seasonal incidence.—Amœbiasis, in general, does not exhibit that seasonal incidence which is so characteristic of bacillary dysentery. Cases may occur at all times of the year, though it is doubtless true that certain climatic factors favour the spread of infection, and therefore the incidence of the disease. Thus, Wagner (1935), in observations extending over eight years, found susceptibility of laboratory animals to infection generally higher during the summer than during the [illegible] on [illegible] nd [illegible] of

Cyst-carriers.—The cyst-carrier, cyst-passer, or cyst-excretor state

not suffered from dysenteric symptoms and who appears in every respect normal. It is postulated from what is known about the natural history of E. histolytica that such a person has living entamœbæ in his tissues. The *convalescent* carrier, on the other hand, is one who

SEX INCIDENCE

Sex	Amœbic *Dysentery* (257 cases)	Liver *Abscess* (169 cases)	*Total* (426 cases)
Male	90 6	97	93 8
Female	9 4	3	6 2

The youngest case the author has treated was a boy aged 7½, seen in April, 1937 He had been in Nyasaland since his ninth month. First attack of amœbic dysentery at one year Three severe relapses treated by emetine ... *during which three* ... cysts in fair numbers ... E.P I. (gr. 18) and ... no more *E. histolytica* cysts seen Permanently cured.

Amœbiasis in native children is probably by no means uncommon It is improbable that they can contract it while being breast-fed, a period which may be considerable, after that, however, they have ample opportunities. H M Perry and H. J. Bensted (1929) have shown that amœbiasis in infants occurs commonly among the poorest inhabitants in Cairo, especially after weaning. According to their statistics, *E histolytica* was found in 13 9 per cent of infantile ... *recorded a case of amœbic dysentery*

cases under 20 -

Thus it may be concluded that, when acute dysentery occurs in children, it is usually of the bacillary form, and that liver abscess is extremely rare under ten years of age, probably on account of the lower incidence of amœbiasis in early childhood C. F. Craig states that the rarity of amœbiasis in children is not due to any inherent insusceptibility to infection, but to a lessened chance of contracting it In family infections, which are not infrequent in the southern United States, it has been shown that even the youngest children are affected, provided they are not breast-fed. The surveys made by E C. Faust and E. S. Kagy in New Orleans, by D F. Milam

J. J. Sapero and C M. Johnson 9.5 per cent. in naval personnel in the

New Orleans. Asylum patients are usually heavily infected; R. M. Svensson (1928) gives 21.4 per cent. in 1,244 lunatics. Food handlers have received special attention, thus A. A. Philiptschenko (1930) found infection rate of 27.7 per cent. in 400 workers in Leningrad H. W. Y. Taylor (1939) reported that six students in the Medical College in Mukden were attacked simultaneously with amœbic dysentery and the cook was found to be a carrier

The incidence of cyst-passers may be taken as an index of the prevalence of amœbic dysentery in a community. Naturally the number of

to 15 per cent.

piled from various sources it as complete as possible occurs in the incidence of

TABLE IX

	Total number of cases examined	Percentage of stools showing E coli.	Percentage of stools showing E.histolytica
England.			
(1) Troops invalided from Gallipoli, 1915	971	30 1	23 7
(2) Civilians (Dobell)	3,146	36 0	7.1
(3) Royal Infirmary, Liverpool	450	6 7	1 5
(4) Recruits in camps	1,098	18 2	5.6
(5) Children under twelve (never out of England)	548	11 1	1.8
(6) Asylum cases (Smith and Malins, 1918)	207	45 9	9.7
(7) Convalescent dysenteries (Matthews and Smith, 1919)	2,355	29 3	13 0
China.			
(1) Chinese and foreign in Peking (Faust, 1929)	13,617	24 2	20 3
(2) Chinese only in Peking	368	30.9	29 5
(3) Foreigners; all ages (Kessel and Svensson, 1924)	818	17.6	14 1

has recovered from an attack of amœbic dysentery and still continues to pass cysts of *E. histolytica* without presenting obvious signs of the disease.

It is now generally understood that for one individual who is suffering from amœbic dysentery and is passing in his stools active vegetative forms (which are non-infective) there are many who continue to pass cysts and constitute a perennial source of infection. The lesions of the mucosa in these individuals may be minute, so as to be visible only in microscopic sections of the bowel. Thus, in a post-mortem on a case of pernicious anæmia in Vienna, J. Hammerschmidt (1919) was able to demonstrate, in serial sections of intestine, invasion of the otherwise undamaged mucosa by amœbæ, although neither the clinical history nor the gross pathological picture suggested amœbiasis, nor could any lesion be detected by the naked eye.

There are certain considerations in the genesis of the carrier state which must be borne in mind. C. Dobell (1919) and many others have observed that no hard-and-fast line can be drawn between the typically healthy carrier and the patient suffering from acute amœbic dysentery. These may be regarded as extreme manifestations of one common condition and interconnected by intermediate states which

the complete absence of dysenteric symptoms. Death may even supervene without suspicion of the disease, as in cases noted by the author in the last war, reported by J. M. Cowan and H. Miller (1918) and later by C. C. Lund and J. R. Ingham (1938), who have recorded four such cases.

C. F. Craig has defined the carrier as an individual in whom *E. histolytica* is living as a *commensal*. In every carrier, cytolysis and superficial necrosis of the intestinal epithelium continually occur in microscopic areas of the intestine; in the majority of cases this is followed by rapid regeneration of the epithelium, but in some cases definite ulceration occurs.

C. A. Hoare (1925) was able to demonstrate a similar state of affairs in kittens artificially infected with *E. histolytica*. When killed forty-one days afterwards, the intestine appeared to the unaided eye to be normal.

... from infection is apparently not dependent on social status

It has been pointed out by several of the above-mentioned observers, who have made a systematic review of this subject, especially by R Svensson (1924), that the incidence of intestinal infection with *Entamœba coli* may afford some indication of the probable rate of infection with *E. histolytica*, indeed, from a consideration of results of research which appear from time to time, it seems that *histolytica* infection may be proportionate to the degree of infection with other intestinal protozoa

On the whole, in making these surveys, less satisfactory results are obtained from examination of formed than of loose motions

Geographical Distribution of Amœbiasis

Until comparatively recent years it had been supposed that amœbic dysentery was a disease confined to the tropics and a limited area of the subtropics, but since more exact observations have been made, and since it has been the practice to examine systematically large numbers of stools for evidence of protozoa, the range of amœbic

where insanitary conditions co-exist with a tropical climate it is found in its most intense form

Although the relatively greater frequency of amœbic dysentery in tropical populations follows naturally upon the greater incidence of infection with *E histolytica*, this does not explain the whole story, for it is well recognized that certain complications of amœbic dysentery, especially liver abscess, are more common among Europeans in the

proximity of Indian troops, who were heavily infected

Amœbiasis becomes more common as the regions of southern Europe are reached and it is now known to be comparatively frequent in South Spain, Italy, the Balkans, Greece, Rumania, and South Russia In

TABLE IX—*continued.*

	Total number of cases examined	*Percentage of stools showing E. coli*	*Percentage of stools showing E. histolytica*
Java.			
(1) Natives (Brug)	150	—	23 6
(2) Europeans (Brug)	*100*	—	27.8
Malaya.			
(1) Malays and Chinese (Jepps, 1923)	1,034	14 5	7.7
India.*			
Egypt.			
(1) Hadra prisoners (healthy) (*Wenyon and O'Connor*, 1917)	524	48 6	13 7
(2) Native cooks (Wenyon and O'Connor)	87	20.7	11.5
C. and S. America.			
Brazil. Amazon school children (Young, 1922)	249	36 9	22 5
Colombia. Santa Maria (Kofoid, 1926)	—	41.1	53.7
Panama (Faust, 1930)	—	26 8	19 2
Porto Rico (Faust, 1934)			
United States.	—	34.2	14 5
(1) Miscellaneous cases (Boeck and Stiles, 1923)	8,029	24 5	6 8
(2) Richmond, overseas troops	2,300	43 6	29 1
(3) Home service troops	*576*	*33 9*	*9.7*
(4) Minnesota (Riley, 1929)	500	16 1	1.9
(5) Wise County (Faust, 1930)	460	55 5	45.4
(6) New Orleans (Faust, 1930)	172	34 0	27 9
(7) Pennsylvania (Freshman, 1933 Warwick *et al*)	—	13 9	4 1

* There are no reliable statistics for the carrier rate in India, those which are found in the literature refer to Indian troops serving in Mesopotamia W MacAdam (1918) gives the following figures —

Previous history of dysentery or diarrhœa
Cases, 218 Carriers, 41 = 18 9 per cent *E histolytica*

Madras

as 21 9 per cent

prophecy in regarding ulceration of the colon and liver abscess as cause and effect.

R. Saundby and J. Miller (1909) recorded a case of amœbic dysentery with abscess of the liver in an inhabitant of Birmingham. Amœbæ were said to have been identified in the abscess, which was situated in the posterior portion of the right lobe of the liver and measured 5 in in diameter.

In 1912, D. G. Marshall recorded a case of indigenous amœbic dysentery in a ploughman aged twenty-six, living near Dunbar, Scotland He suffered from chronic diarrhœa and was successfully treated with ipecacuanha. Amœbæ were said to have been found in the stools.

C M. Wenyon (1916) recorded a genuine case of amœbic dysentery in the London Hospital This was a labourer who had never been out of England and who apparently had contracted the infection while working on a transport lying in the London Docks A liver abscess was subsequently opened and drained, and in scrapings of the wall active *E histolytica* were found, at the post-mortem a second liver abscess was disclosed, and there were amœbic ulcers in the large bowel In the same year two further cases were recorded by G C Low and C Dobell.

A. [illegible]

case [illegible]

The [illegible]

absce [illegible]

In 1[illegible]

dysentery in an attendant of the Burnley (Lancs) public abattoir Open operation was performed, but the patient subsequently died.

The author, with C B. V. Tait (1929), recorded yet another case of indigenous amœbic infection This man, a stevedore, aged sixty, was seen at the Albert Dock Hospital in 1928 He had never left this country, but for forty years had worked on ships from Calcutta and Bombay, and it was from this source that he had probably contracted the infection Numerous and active *E histolytica* were found in the blood-and-mucus stools He had then been ill for over two years with very evident signs of dysentery, and had been treated as a case of lead poisoning Response to anti-amœbic treatment in his case was instantaneous

France.—M Gaillard and M Brumpt (1912) recorded a case of amœbic dysentery of three and a half months' duration in a man of [illegible]

[illegible]

Army. Free and encysted amœbæ were found in the stools, and a kitten injected with material per rectum became infected and died L Landouzy and Debré (1914) described a fatal case of amœbic dysentery

Asia Minor, Palestine, and particularly in North Africa from Egypt to Morocco, amœbic dysentery and liver abscess are endemic, while throughout the whole of tropical Africa, especially on the West Coast, on the Congo, and in British East Africa, this desease is relatively common; the author has seen indigenous cases as far south as Cape Province.

In Asia, there is abundant evidence that amœbiasis is prevalent in

America, and it appears to be relatively frequent in the southern United States, especially Texas and South Carolina. In Mexico, Panama and the northern half of South America—Venezuela, the Guianas, and Brazil—it appears to be as freqnent as in Asia, and extends as far south as Paraguay and northern Argentina; though from farther south there appears to be no record of the disease. In northern America amœbic dysentery and liver abscess are by no means rare

of transmission.

Amœbic dysentery is well established in most islands, occurring

Islands and New Zealand appear to be exempt. It is probable that more extended enquiries will show an even more widespread endemicity.

England.—From a perusal of the extensive literature on this subject, little doubt can remain that from time to time genuine autochthonous cases of amœbic dysentery and liver abscess actually do occur in the British Isles.

In the older records are two cases cited by Dickinson. The first was

Hospital. In discussing

prophecy in regarding ulceration of the colon and liver abscess as cause and effect.

in diameter.

In 1912, D. G. Marshall recorded a case of indigenous amœbic dysentery in a ploughman aged twenty-six, living near Dunbar, Scotland. He suffered from chronic diarrhœa and was successfully treated with ipecacuanha Amœbæ were said to have been found in the stools

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dysentery in an attendant of the Burnley (Lancs) public abattoir

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France.—M. Gaillard and M Brumpt (1912) recorded a case of amœbic dysentery of three and a half months' duration in a man of twenty-eight who had never left France; amœbæ were found in the stools. J. Paviot and C. Garin (1913) in Lyons recorded a fatal case in a man who had never been out of France and who had not served in the Army. Free and encysted amœbæ were found in the stools, and a kitten injected with material per rectum became infected and died L. Landouzy and Debré (1914) described a fatal case of amœbic dysentery

in a bargee on the Seine, and Labbé (1919) eight cases of indigenous amœbic dysentery in Paris.

P. M Rennie (1922) has recorded five of the author's cases of amœbic dysentery in returned soldiers who originally contracted their infection in France. C. Garin and P. Lépine (1924) consider that amœbiasis *was introduced into France on a large scale by Colonial troops during* the last War They have collected a series of 208 cases and two indigenous cases of liver abscess, in less than four years, all in the vicinity of Lyons

Germany.—Jurgens (1908) first recorded indigenous amœbic dysentery in Germany in a boy of sixteen at the Charité Hospital in Berlin W. Fischer (1920), in Berlin, recorded two genuinely indigenous cases—a young man who had suffered from clinical dysentery in the Army, and a young woman who was passing blood-and-mucus stools containing *E. histolytica*, with ingested red blood-cells. The author treated two cases of amœbic dysentery in returned soldiers who contracted the infection as prisoners of war in Germany.

F. W Bach (1932) examined the fæces of 1,000 subjects for parasitic protozoa in Germany and found *E. histolytica* cysts in 5.7 per cent.

Norway.—J Bøe (1940) has described an indigenous case of *E. histolytica* infection in a woman who had never been out of Norway and the disease was reproduced by intrarectal injection of the cysts into kittens

Russia.—The records from Russia are scanty, but it must not be [illegible] disease after heroic efforts The patient was first seen in [illegible] by Losch by injection of [illegible] which lies well within the Arctic Circle, G. V Epstein (1931) found a carrier rate of 60 6 per cent. in 900 persons, but not a single case of amœbic dysentery.

According to recent surveys amœbiasis appears to be widely spread through Soviet Russia. The figures are as follows:

	No of cases	*Percentage of E. histolytica*
Leningrad	1,404	25 3
Kola Peninsula	900	60 6
Azerbaijan	1,146	32 5
Armenia	—	17.7
Georgia	570	32.3
Turkestan	1,664	25

Hungary.—G. Bodrogi and G. Makara (1939) found in one village 22 per cent and in the Government Hygiene Institute 28 per cent

Holland.—W. A. Kuenen (1918) quoted seven cases of amœbiasis contracted in Holland, in four of which there were intestinal symptoms, with active *E histolytica* in the fæces; and re-cited the case of Nolen, who in 1908 had medical care of a Dutch fisherman from Vlaardingen, who was passing blood-and-mucus stools with amœbæ containing ingested red blood-cells

J. van der Hoeven (1921) treated a case of indigenous liver abscess in a woman aged thirty-nine, who had never been out of Holland. Amœbæ were demonstrated in the evacuated pus

E P. Snijders (1929) discovered a family in Holland of which three members had suffered from amœbic dysentery

[illegible]

country, and in the same year there appeared an exhaustive study by W T Councilman and H. A Lafleur, a description of the

[illegible]

amœbiasis in the northern United States, and in a microscopic examination of 13,043 fæcal specimens of 8,029 persons and in 28 institutions, found that 39 9 per cent showed protozoa, and 4 1 per cent *E histolytica* Of 2,584 soldiers who did not go to Europe, 3 5 per cent were infected, and of 3,536 soldiers who returned thence 2 8 per cent were infected The practical facts, he states, are as follows "In temperate climates the intestinal protozoa of man are

[illegible]

origin observed in the Mayo clinic They comprised 153 cases with dysentery or liver abscess, 258 cases in which the chief complaint was diarrhœa, and 122 "carrier" cases The best treatment was found to be the generally recognized anti-amœbic treatment, with dilute hydrochloric acid for achlorhydria (This appears to be an

occasion where achlorhydria has been noted in amœbiasis—a fact which requires further study.)

the Chicago Board of Health averaged one or two cases monthly. On August 15, 1933, two cases were reported in which the patients had eaten a meal at a certain hotel, and subsequently, with great promptitude, 864 food-handlers at this hotel were investigated, with the result

cysts in their fæces (The epidemic has already been reported on p 122.)

It appears probable, from the work of W. E. Frye and H E Meleney (1933), that strains of *E. histolytica* in the United States may vary greatly in virulence. C. F. Craig (1935) has collected together the statistics which have been amassed The positive

first category 2.8 per cent were infected; in the second 3 5 per cent.; in the third 8 8 per cent, and in the fourth 3 per cent.

mœbic

intry,

Central and South America.—From the writings of W. M. James and W. E Deeks (1924) it is known that amœbiasis is widespread in the *Panama zone*

In *Colombia*, W. M. James (1925) found over 50 per cent. of hospital patients infected with *E. histolytica*. Among club servants, waiters and cooks an astonishing incidence of 60 per cent. was revealed In out-patients with past histories of dysentery more than this number

India.—Amœbiasis appears to be widespread throughout the Peninsula. It is difficult to state with any degree of accuracy the proportion of the population affected as, from the writings of J. A.

Manifold (1926), there appear to be considerable differences of opinion in this respect (*see* p 27); this subject was dealt with under the section devoted to the carrier problem (p 128).

China.—J. F Kessel and O Willner (1925), in the Peking Union Medical College, record that out of 1,600 patients admitted, 7 per cent were found to be suffering from amœbiasis; 16 7 per cent of the Chinese so infected and 30 per cent of the foreigners were suffering from acute or chronic colitis, while 34 4 per cent. of Chinese cases and 9 per cent. of foreigners were symptomless and apparently healthy "carriers"

Dutch East Indies.—From the writings of P C Flu (1919) and S. L. Brug (1920), it is known that amœbiasis is a common disease in these islands, the former finding 10 5 per cent., the latter 12 7 per cent of the inhabitants infected, while F H Ter Poorten (1928) records that of European naval ratings returned from service in these waters about 10 per cent. were found infected with *E. histolytica*.

Australia.—Amœbiasis is indigenous to the whole continent of Australia The author treated a severe case of intestinal amœbiasis [illegible] never left the country.

The relative incidence of the two main forms of dysentery, as summarized in various official reports, is given in Table X, p 136.

TABLE X*

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
EUROPE — France	1917	Leygue, G, and Haguenade, J	S of Somme	449	—	Shiga, 30, Flexner, 5, Hiss, 20	Army
	1917	Lancelin, R, and Rideau, I	Brest	202	8	Shiga, 27, Flexner, 102	Prisoners of war
	1918	Stockey, G E	Bertichamp, Meurthe Moselle	—	—	Flexner Y	Civil population
	1918	Florand, Bezançon, and Paraf	Nr. Paris	230	—	Shiga, 43	Military camp
Belgium	1920	Keesmakers	Brussels	170	—	Flexner	Army garrison, June to Sept
Germany	1915	Matthes, M	—	—	—	Bac. dys Y	Army. Mild epidemic. Relapses frequent, often worse than initial attack
	1917	Mayerhofer, E., and Von Reuss, A.	Baden Leesdorff	221	—	Shiga Kruse	Civil Fatal cases mostly in children and old people
	1917	Laempe, R	Dresden	—	—	Dys bac. found in 15% of cases	All ages
	1918	Abel, R, and Loeffler	—	—	—	Shiga Kruse	Res. batn. Landstürm *Origin traced to* potato salad; out of 1,360 persons who ate it, 27 61% attacked

* Much of this information has been obtained from the Epidemiological Report of the League of Nations, 1933.

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
Germany	1928	Buchner, S	Münster	160		Bac dys in half the cases over 6 mths of age, in nearly all over 2 yrs	—
Austria	1920	Bernstein, S, Kling, D, and Rosenblatt, S	Vienna	901	4%	Shiga, Flexner Y, and Strong in 65%	During and after war
Russia	1916	Meyer, F	—	—	—	Third of cases developed fever, 10 cases, Flexner Y	Army
	1916	Koch, J	—	—	—	Bac dys epidemio	War time
	1930	Philiptschenko, A A	Leningrad	225	—	Bac dys in 9 8% of cases	Epidemiological Rept of R S F S R (1933) shows bac dys to be prevalent in European Russia to extent of 0 434 per thousand of inhabitants
Italy	1928	Official statistics	—	—	594	55 deaths due to amœbiasis, 72 to bac dys	Bac dys predominates throughout country
Spain	1929	Garcia, E	—	—	800–900 per ann	Majority bac	Civil population
Yugoslavia	1919–25	—	—	Decline from 17,532 to 1,311 per ann	—	Bac dys	Civil population

TABLE X (*Cont.*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc)
BULGARIA	—	—	—	500 per ann	—	Bac dys	Civil population
RUMANIA	1932	—	—	7,285	*860*	*Chiefly bac dys*	*Civil population*
GIBRALTAR	1932	Colonial laboratories	—	—	—	—	In the Colonial lab, bac dys alone reported amongst European population
CYPRUS	1927–31	Colonial laboratories	—	132–837 per ann	—	Bac and amœb. dys. about equal	Civil population
	1930–31	Colonial laboratories	—	52 in 1931	—	Shiga	„ „
AFRICA — EGYPT	1902–27	Khouri, J	—	—	—	Bac. dys prevailing form, 65% of cases Shiga and Flexner	Civil population
	1930	—	—	2,207	532	Bac dys	„ „
SUDAN	1930	Official statistics	Khartoum, N Khartoum and Omdurman	1,522	—	Bac dys, and amœb (amœb prevailing 8 : 1)	—
	1931	Official statistics	—	81	—	Flexner, 37, Shiga, 28	—
	—	Riding, D			—	Para Shiga bac. of Schmitz	Outbreak among Brit. officials
SOMALILAND	1929–31	Official statistics	Brit territory	259	—	Bac. dys predominates. 3 cases intestinal amœbiasis	—

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
E Africa	1917	Pirie, J H H	—	56	—	Shiga and Flexner 2 cases, *E histolytica*	E African Expeditionary Force
Kenya	1931	Official statistics	—	1,233	34	35 2% bac dys, remainder amœb	Civil population
Uganda	1931	Official statistics	—	5,365	—	65 7% bac dys	—
Tanganyika	1929–31	Official statistics	—	3,031	—	25% bac dys, 75% amœb	Bacillary infection probably more prevalent than indicated
Nyasaland	1931	Official statistics	—	2,270 (60 Europeans)	—	Definite nature of infection ascertained in only 319 cases, 50% bac dys	Civil population
Zanzibar	1930	Official statistics	—	156	9	Bac dys	Prison epidemic Suggested transmission by houseflies
	1931	—	—	151	—	95 cases bac dys, 5 amœb	—
Seychelles	1931	Official statistics	—	73	7	Bac dys, 6 amœb cases	Suggested introduction by carrier from E Africa
Mauritius	1921	Balfour, A	—	11,073	—	499 deaths attrib. to dysentery, 308 to diarrhœa	Civil population

TABLE X (*Cont*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc)
MAURITIUS ..	1931	Official statistics	—	—	—	Shiga, Flexner, Hiss and Russell	Civil population
MADAGASCAR	1932	Ledentu	—	5,894	112	Chiefly bac dys, 8 cases amœb	Civil population
	1928	Robic, J	—	—	—	Chiefly Shiga and Flexner	Previously dys had been considered amœbic in type
RHODESIA .	1931	—	Roan Antelope and N'Kana Mines	71 Europeans, 115 Natives	13 27	Amœb. and bac dys Amœb. more prevalent	Mine workers
BASUTOLAND	1931	Official statistics	—	161	114	Bac dys	Specially fatal in Leper Colony (18 deaths)
UNION OF S AFRICA AND S W AFRICA	1928-31	Official statistics	—	—	3 per 1,000	—	Population of 7,000 miners
	1930	Brink, C D, Campbell, W, MacFadyen, J. A, and Claasens, J D.	—	—	—	Amœbiasis 4½ times as prevalent as bac dys	—
	1929	Fischer, W. O.	Rand	—	—	—	In 1402 post-mortems on native miners, amœbic dys lesions found in only 15 cases, liver abscesses in 4
BELGIAN CONGO	1930	Official statistics	—	126 Europeans	—	10 bac. dys., 116 amœb.	—
				3,113 Natives	—	47 bac dys, 3,039 amœb.	—

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc.)
Belgian Congo	1930	Official statistics	Kasai provinces	6–8% of pop	40%	Shiga predominant	—
	1930	Pergher, J V and Van Riel, J	Eastern provinces	12,000 Natives	—	Shiga predominant	—
	1925	Official statistics	Katanga, Panda	462 Natives	80	Bac dys	—
		Van Hoof L	—	—	—	—	Sporadic outbreaks coinciding with famine
French Congo	1928	—	—	155	—	All types, Shiga, 21 9%	—
Nigeria	1925	Connal, A, and Smith, E C	—	—	—	—	Reported autopsy findings of what they considered to be first case of bac. dys More accurate records 1929–31 Amœbic form predominates
	1930	Official statistics	—	218 Europeans	—	164 amœb, 32 bac	—
				3,374 Natives	—	2,893 amœb, 285 bac	—
	1931	Young, J A	—	4,385	—	128 bac dys, 22 Flexner	—
Gold Coast	1929 31	Official statistics	—	3,968 Natives	7 7%	20 3% bac dys	Amœbic form predominates
Liberia	1930	Strong, R P	—	—	—	Amœb and bac dys	Dysentery rarer in Liberia than in many tropical countries
Sierra Leone	1930	Official statistics	—	777	—	4 cases of bac dys	No full time pathologist Identification uncertain

TABLE X (*Cont.*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc.)
GAMBIA	1929-31	Official statistics	—	63	—	4 cases of bac dys	No full-time pathologist Identification uncertain
FRENCH W AFRICA—							
Senegal	1930	Official statistics	—	1 020	—	Bac dys	—
Mauritania	1930	Official statistics	—	667	—	Bac dys	—
French Sudan	1930	Official statistics	—	281	—	Bac dys	—
Ivory Coast	1930	Official statistics	—	5,170	—	Bac dys	Dock workers
ALGIERS AND TUNIS	1930	—	—	—	—	0 19 per 1,000 bac dys, 0 9 per 1,000 amœb Amœb dys more prev. in Tunis	Civilian pop. dys. low, military pop higher
N. AMERICA — CANADA	—	—	—	—	—	Bac dys. predominates	Relatively rare
U S A. (NORTH)	—	—	—	—	—	—	Relatively rare Only sporadic cases of amœbic dys. are found
Boston ..	1930	—	—	30	—	Sonne	Children
California	1928	—	United Fruit Co	82	8	—	—
	1928	Stanley, L. L., Garfinkle, F E., and Goddard, W. P	—	946	—	Flexner	Prison
	1928	Lommell, J.	—	—	—	Sonne	Child (mild dys.)

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
U S A (South)	1930 1931 1932	Meleney, H E Milam, D F Meleney, H E, Bishop, E L, and Leathers, W S	—	—	—	Bac dys rare	Few statistics available
CEN AMERICA British Honduras	1930–31	Official statistics	—	166	—	—	Hospital No differentiation
Costa Rica	1932	—	—	907	70	Amœb	—
Panama	1931	—	—	16 302 Hosp cases	—	Bac dys 4 cases majority amœb	—
Leeward Is *Antigua* *Dominica* *St Christopher* *St Nevis*	1931	Official statistics	—	—	106	Infection not recognized Considered amœbiasis	Children
Windward Is	1928–30	—	Grenada	164, 34, and 16 respectively	—	—	—
Bahamas	1930	—	—	—	—	Bac dys, no amœb	—
Barbados	1931	—	—	—	107	Bac dys, no amœb	49 deaths in children under 5
Jamaica	1931	—	Kingston (Hosp)	16	3	No mention of amœbiasis	—

TABLE X (*Cont.*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc)
TRINIDAD .	1931	—	Coura District	322 (Hosp)	—	20 cases recognized as bac dys	—
HAITI	1930	—	—	—	—	—	Information unsatisfactory .
PUERTO RICO	1928–29	—	—	6,473	717	Bac exam in 137 cases only Flexner's bac found	—
S. AMERICA BRITISH GUIANA	1919–31	—	—	200 per ann	16–19 per ann	No differentiation recorded	Records unsatisfactory
DUTCH GUIANA	—	Flu, P C	Surinam	—	—	Amœb.rare. Bac. dys. only in small epidemics	
BRAZIL ..	1927	Bernd, M , and Bachman, N	Northern provinces	—	—	Amœbiasis	Records unsatisfactory
	1929	Vieira, F B	Southern provinces	—	—	Bac. dys	—
	1931	De Assis and Mendes	Rio de Janeiro	153	—	Flexner predominant (Flexner 74 5%, Shiga 20 9%); Sonne	In 1929 epidem , chiefly children
		De Mendonca	São Paulo	—	—	Majority bac. dys.	—
ARGENTINE	1930	Public Health Reports	Buenos Aires	804	—	Bac. dys , 27.4% ; Flexner, 73 6%; Shiga, 21% ; Sonne, also found	Civil population

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
Chile & Peru	1932	Garces, C	—	—	200-300 per ann	Amoeb in adults, bac dys in children	Records few
Australia	1931	Brown, J., and Hickey, G V	—	—	—	Bac dys except in N territory, Sporadic cases of amœb only	Incidence low
	1931	Burnell, F M, McKie, M, and Wood, I J	—	—	95	56 deaths, bac dys Maj of bac dys cases in children Flexner, some Sonne	Civil population
New Zealand	1932	Official statistics	—	45	10	Bac dys	Civil population
Oceania New Guinea, New Britain	—	Official statistics	—	—	—	Mostly bac dys, but some amœb	Epidem dys
Papua	1932	Official statistics	—	471	138	Bac dys	
Bri Solomon I	1928	Crichlow, N	—	—	Heavy	Bac dys	Endemic and epidemic
New Hebrides, New Caledonia	1930	Official statistics	—	—	—	Bac dys (amœb 9 7%)	—
Fiji Islands	1912	Official statistics (Bahr, P H)	—		—	Bac dys, Shiga and Flexner	Epidemic (amœbiasis endemic)
	1929–30	Official statistics	—	698 (Hosp)	—	Shiga predominant	Epidemic 1929–30
	1931	—	—	—	—	Shiga predominant	Similar outbreak

TABLE X (*Cont*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc)
GILBERT AND ELLIS I	1930-1	—	Funafuti	—	—	Bac dys	Civil population
		Official statistics	W Samoa	—	—	Bac dys. due to Shiga	,, ,,
		—	Tonga Isl	—	—	Bac dys	
HAWAIAN I	1932			2	—	Bac dys rare	
ASIA— PALESTINE	1919	Manson-Bahr, P H	—	—	—	Bac. dys prevalent. Some amœb in native troops	Expeditionary Force Seasonal curve
	1927	Kligler, I J, and Weitzman, I	—	—	—	Bac dys, out of 65% stools, 35% bac. dys	Civil population
	1927	Olitzki, L, and Reich, K	—	—	—	Bac. dys.; amœb in summer	Seasonal epidem, peaks spring- and autumn 20% in children, 6 mths–2 yrs.
	1927	Official statistics	—	1,782	—	25 % bac. origin	
	1931	,, ,,	—	297	—	Bac. dys.	
TRANSJORDANIA	1931	Official statistics	—	28 (examd)	—	25 bac. dys.	
SYRIA	1931	—	—	—	—	Bac. dys. rare	Sporadic
IRAQ	1917-18	Ledingham, J. C. G.	Mesopotamia	715	—	Shiga 45 3%, Flexner, 54 7%	Spring and autumn. Incidence greater in Brit. than in Indian troops
	1927	Shelton, D S, Malcolm, J. W, and Lloyd, R.	Mosul area	—	—	Bac. dys.	—
	1925-26	League of Nations	—	54,161	—	Diarr and dys	Civil population

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
India	1930	League of Nations	—	—	—	64 6% bac dys, amœb 8 4% Ind, 15 6% Brit, Flexner, 77 6%, 15 7%, Sonne 2 2%	Brit and Indian troops
	1927	Large, D T M	Lahore	—	—	80% bac dys, mostly Shiga, 20% amœb	—
	1922	Official statistics (Army)	—	573	—	479 protozoal, 16 bac	—
				318	—	303 protozoal, 6 bac, 9 unclassifd	—
	1923	Cunningham, J	E Bengal	—	—	86% bac dys	Prisons
		Official statistics	Madras Presidency	—	—	86% bac dys	Prisons (Moplah Rising)
	1920–23	Acton, H W and Knowles, R	Calcutta	—	—	Bac dys amœb 5 1	—
Ceylon	1929	Colonial Office Reports	—	5,909	—	4,478 (75 8%) amœb, 1,429 (24 2%) bac dys	Civil population
	1929	Official statistics	W Province	40 365 out pts 7,242 in pts	3,616 1,652	Majority Flexner	—
	1931	—	—	489	—	383 (78 3%) bac dys	Sporadic Higher in W Province
Siam	1925–26	—	—	6,016	—	Of 1,847 stools exam 22 amœb	—
Malaya	1916	Fraser, H	—	—	—	—	—
	1924	Fletcher, W, and Jepps, W	—	—		80% bac dys	Bac and amœb equal in Fed Malay States

TABLE X (*Cont.*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc.)
MALAYA	1930	Official statistics	Federated Malay States	1,735	—	866 bac, 869 amœb	—
	1930	" "	Kedah	259	—	99 bac, 160 amœb	—
	1930	" "	Kelantan	54	—	6 bac, 48 amœb	—
	1930	" "	Trengganu	37 Hosp.	—	4 bac, 29 amœb, 4 *undefined*	—
STRAITS SETTLEMENTS	1929	Official statistics	—	1,167 Hosp	—	290 bac, 531 amœb.	Civil population
	1931	" "	—	—	249	117 bac., 103 amœb 23 undefined	" "
	—	" "	Singapore	234	—	10 bac, Shiga 3, Flexner 16, Hiss and Russell 6	" "
DUTCH E. INDIES	1919	Baerman, G.	—	0.8 per 1,000	—	Amœb.	Plantation coolies
	1925	"	—	0.7 per 1,000	—	Bac dys.	" "
	1927	Wolff, J W	Sumatra	—	—	—	Increasing import. of bac. dys. as factor
	—	—	Java and Celebes	—	—	Bac. dys. noted. Amœb dys endemic	—
	1932	"	Java and Madura	698	81	—	—
	—	"	Celebes	135	—	—	—
	—	"	Timor	40	—	—	—
BORNEO	1931	—	Kuching (Sarawak)	615	36	Bac. dys.	—
	—	—	Brunei	9,947	164	Bac dys.	Population of 24,000
				197 (Hosp)	—	9 bac. dys, 3 amœb	—

Country	Date	Observer	Place of Epidemic	Number of Cases	Deaths	Type of Dysentery	Type of Epidemic (Age, Army, Prison, etc)
Philippine I	1926	Allison, I, and Quaison, J O	—	136	31 0%	Flexner bac	May-October
	1928		—	11,056	4,532	2,074 amœb, 1,987 bac dys	—
	1928	Mendoza - Guazon, M P	Manila	—	132	14 amœb, 50 bac dys	Epidemics frequent in rainy season
	1929	Corpus, G	Manila	200	76	Shiga, Flexner & Morgan's	Children chiefly
China	1931	—	Hong Kong	115 Govt Hosp	3	57 amœb, 47 bac dys.	Civil population
				598 Chinese Hosp	40 amœb 10 bac dys	146 amœb, 48 bac dys	″ ″
						Flexner predom Shiga rare	″ ″
	1932	—	Shanghai	99 amœb 122 bac dys	5 amœb 8bac dys	—	Foreigners
	1931	—	″	—	—	660 stools dys Majority Flexner or Sonne, 72 Shiga	Bac dys more frequent in towns
	—	—	Central China	—	—	Amœbiasis chiefly	—
	1930	Smyly, H J, and Lee, S W	Peiping	—	—	Bac dys	—
				38	—	28 bac dys, 7amœb Several mixed	Complicating puerperium
	—		S Manchuria	—	—	Bac dys to amœb 34 1	—

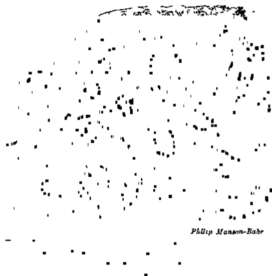
TABLE X (*Cont.*)

COUNTRY	DATE	OBSERVER	PLACE OF EPIDEMIC	NUMBER OF CASES	DEATHS	TYPE OF DYSENTERY	TYPE OF EPIDEMIC (Age, Army, Prison, etc.)
CHINA	1928	Hoshijaki, S.	Dairen	1,220	54 9%	1,114 Japanese, 106 Chinese Hiss and Russell 46 1%, Shiga 39 3%, Flexner 5 6%, Others 9 1%	Chinese mortality three times as high as Japanese
	1927	—	—	—	24 4% (Shiga) 39 4% (Others)	—	Toxic symptoms less marked in Shiga
	1928	Tsuchiya, K., and Nagata, S.	—	—	—	—	Shiga commoner in children over 7
JAPAN	1929	—	—	—	3,166	Bac. dys. predominant	Acute type in children under 5 (*Ekiri*)
	—	—	—	—	10,261 (*Ekiri*)	—	Female deaths exceed males; Incidence higher, July–Sept
	1927	Mitsuhashi, C.	—	36	—	—	Women's School
	1926	Sasaki, R.	—	30	—	Bac. dys., Flexner chiefly	Fulminating cases

CHAPTER XI

AMŒBIASIS (*continued*): PATHOLOGY, MORBID ANATOMY, SYMPTOMATOLOGY AND COMPLICATIONS

The pathological appearances of intestinal amœbiasis, so intimately connected with the activities of *E histolytica*, naturally vary enormously in their extent according to the severity of the infection and resisting power of the host. As far as is at present understood, the mature, living cysts of *E. histolytica*, when swallowed, pass into the stomach and are not affected by the gastric juices, it is not until they



reach the small intestine that the cyst-walls are dissolved and the liberated amœbæ pass with the intestinal contents into the large intestine, where they establish themselves. Amœbic dysentery is thus [illegible]

of Lieberkuhn and, penetrating the basement membrane, gain entrance to the submucosa. Here they attack and invade the tissues, both by their own activities and by means of a powerful cytolytic ferment, as was shown by C Craig (1927) (Fig. 17.)

Soon, by active proliferation, nests of amœbæ form which destroy



Fig. 18 —Section through flask-shaped ulcer, showing amœbæ *in situ*.
(After Craig, from American Army Museum Collection)

ortem examinations on
cent infected and was

able to demonstrate *Entamœba histolytica* in the lesions, which were of [illegible]

Deep ulcers usually have swollen or raised edges and are surrounded by numerous hæmorrhages. The smallest take the form of granular patches on the mucous membrane which are very difficult to see except with a magnifying lens. These ulcerations assume different appearances according to the reaction of the tissues. As a general rule, in contradistinction to the bacillary form, the mucous membrane intervening between individual ulcerations is normal in colour and in texture When large necrotic sloughs form at the base of amœbic ulcers they [illegible]

hilts In less severe cases the ulcers are more superficial and the whole colon may be covered with what are appropriately termed "sea-anemone ulcers," with rounded raised margins and white fluffy bases Solitary ulcers are sometimes seen, and may be found even in the rectum, or again the whole surface of the colon may be covered with a [illegible]

extremely friable

The character of the stool depends to a great extent upon the size and

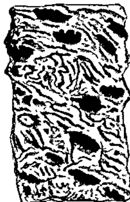
nature of amœbic lesions. When much necrotic tissue is present the fæces are foul and contain greenish sloughs.

Amœbic lesions are especially abundant in certain portions of the bowel, being as a rule most extensive in the neighbourhood of the flexures. When they are very numerous, the mucous membrane of the large intestine may be so undermined and burrowed by ulcers that the surface may resemble a tangle of seaweed (Plate VII, 3)

A. W. Sellards and L. Leiva (1929) have shown that when the cæcum is exposed and material directly introduced into the lumen of the bowel, infection takes place with surprising regularity. Whether introduced into the cæcum or via the rectum, the initial lesions occur in the extreme lower part of the bowel. Stasis occurring in the large bowel certainly affords an opportunity for amœbæ to gain a foothold and is a factor determining the location of the initial lesion. The subsequent dissemination of the lesions indicates that there are no pronounced differences in the susceptibility of various areas of the colon. In dogs, however, E. C. Faust and E. S Kagy found that the cæcum usually constituted the earliest site of an amœbic attack.

The most extensive experimental investigations on the pathology of amœbiasis in cats and dogs and its bearing upon the pathological histology of the disease in man, are those of O. Wagner and R. Bieling (1935), who found that, following both rectal and oral administration of infected material, two points of the large intestine are first attacked :—namely, the lower part of the large intestine immediately above the anal ring, and the region just below the ileo-cæcal valve The amœbæ here enter the tissue in one of three ways, passing directly into the connective tissue, into the crypts, or into the lymph channels, whence they migrate to the lymph follicles and the submucosa. The intestinal mucosa responds to the invasion by an increased production of mucus which, when mixed with blood, forms an excellent medium for the development of amœbæ on the surface of the intestine.

As a rule, ulcers in the rectum are the most minute; hence the necessity of being able to recognize them by the sigmoidoscope. The most extensive work on the distribution of amœbic lesions in the bowel is that by H C Clark in 1924. In 186 fatal cases examined postmortem the lesions were scattered throughout the colon in 61 per cent., and involved isolated areas alone in 34 per cent., affecting, in order of frequency, the cæcum, ascending colon, iliac colon, rectum, and hepatic flexure; in ten cases (5 per cent) no ulcers, but only scars, were found, these being cases of secondary amœbiasis with infection of other organs (Fig 19) As has been already pointed out, stasis is of great importance in intestinal amœbiasis, and, as might be expected, it is at the sites where this is greatest that there is a special tendency for the amœbæ to invade the bowel. Of interest was the fact that the appendix was affected in 41 per cent. of cases, and in 9.2 per cent. perforation or abscess formation had occurred, it being proved by microscopic section in six cases that there were extensive



1, "Dyak-hair" sloughs.



2, "Sea-anemone" ulcers



3, "Seaweed" sloughs.



4, Typical punched-out ulcers with thinning and ballooning of intestinal walls.

PATHOLOGY OF THE COLON IN AMŒBIC DYSENTERY

(*Drawn by P. H. Manson Bahr, after W. Fletcher and M. W. Jepps.*)

PLATE VII



1, Amœbic ulceration of descending colon (proved by sigmoidoscopy and fæces examination). Note ***slight filling defect of cæcum.***



Photo: Dr G. Mather Cordiner.

2, Amœbiasis of descending colon; the same case four years later, showing formation of pericolic abscess.

amœbic lesions Wherever there was amœbic ulceration of the cæcum, the appendix also was involved It must be pointed out that the frequency of appendix lesions in Clark's series appears to be extraordinarily high; most of his autopsies were made in negroes, among whom the incidence of appendix lesions may be higher than in other races, since they possess, as a rule, large appendices with a patent lumen

The distribution of amœbic lesions (primary amœbiasis) in Clark's 186 cases can be best presented in tabular form (Table XI, *overleaf*)

The post-mortem appearances of amœbic dysentery are naturally

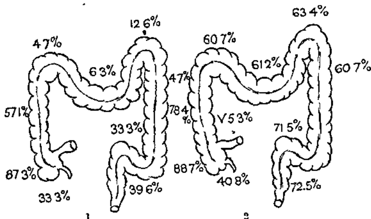


Fig. 19 —Diagrams showing distribution of amœbic lesions in the appendix, colon and rectum. (*After H C Clark*, 1924)

one instance a fæcal fistula and fistula-in-ano were proved to be of amœbic origin Localized peritoneal abscesses, formed by walling-off of the peritoneum in the neighbourhood of perforated amœbic ulcers, have also been noted

Where the blood supply of the bowel has been severely interfered with through thrombosis of the submucous veins and secondary bacterial invasion, extensive gangrene of the mucosa may ensue, followed by sloughing Large areas of the bowel may be involved in

TABLE XI

Distribution	*Cases*
Entire colon	55
Entire colon and ileo-cæcal valve	3
Entire colon and appendix	48
Entire colon and appendix and ileo-cæcal valve	7
Cæcum and ascending colon	24
Cæcum, ascending colon, and appendix	9
Cæcum, rectum, and sigmoid	8
Cæcum, rectum, sigmoid, and appendix	6
No primary lesions found in the intestine or appendix	7
Scar or almost healed lesions in the colon	3
Appendix, cæcum, splenic flexure, and rectum	2
Rectum	2
[illegible]	2
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1
[illegible]	1

this process and the result is invariably fatal. Rarely, the small [illegible]

Biggam [illegible] of the bowel there is little in the post- [illegible]

Histopathology.—The lesions caused by the amœbæ are followed

deeper than the submucous layer, but in some cases the amœbæ may destroy the muscular layers and finally reach the peritoneal coat

The necrotic tissue in the cavity of the ulcer consists of gelatinous coagulum containing cells in all stages of destruction and frequently masses of extruded nuclei, histiocytes (macrophages) being commonly encountered D L. Martin (1930) points out that, beyond the boundaries of the cellular infiltration, the lymph vessels may be found dilated, with their contents coagulated

When the amœbæ have penetrated the fundi of the glands, they

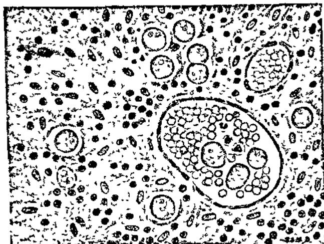


Fig 20 —Microscopic section through the submucosa, showing three amœbæ (*E histolytica*) within the lumen of a vein.

[illegible]

At first there is little or no response on the part of the host, but when bacteria gain entrance to the tissues, marked cellular reaction occurs, and the submucosal lesion takes on the appearance of a pyogenic abscess with few visible amœbæ. Should the lymphatics of the submucosa have been opened up by necrosis, they may become filled with necrotic cells and bacteria—more strikingly in the artificially-produced disease in kittens than in man Although amœbæ enter the lymph-vessels, and are undoubtedly carried to the mesenteric lymph-glands, lesions are practically unknown (H E. Meleney).

Should the patient be a carrier of the cysts of *E. histolytica*, there are a number of ulcers in the bowel; it appears possible, from the observation of W. E. Musgrave, G. B. Bartlett, and other pathologists, that a considerable degree of ulceration may be compatible with good health and may exist in the absence of dysenteric symptoms.

The healing of amœbic ulcers is important and it is necessary to be



Fig. 21.—Section through base of amœbic ulcer, showing *E. hystolytica* in the tissues (*C. M. Wenyon.*)

familiar with their appearances. When separation of the sloughs has taken place, granulation tissue forms on the surface and floor of the

Pathology of amœbiasis in experimental animals.—It has become evident that care must be exercised in drawing conclusions from a study of the pathological conditions in experimental animals. In kittens injection leads to a very acute and rapidly fatal amœbic dysentery, while in the dog it is invariably of the chronic type.

C. W. Rees (1929) found that, of forty-nine kittens which were inoculated with cultures of *E histolytica* directly into the intestines after laparotomy, twenty-three developed lesions, while of thirty seven infected intrarectally fifteen developed similar lesions In kittens directly inoculated after laparotomy, ulcerations could not be found till forty hours had elapsed, but lesions were found after ninety hours, especially near the ileo-cæcal valve R W Nauss and I Rappaport (1940) have made an important observation that invasiveness of *E histolytica* for the intestinal mucosa of kittens is increased by the irritant action of croton oil and that of certain bacteria associated with cultures of *E histolytica*

D L Martin (1930) in a study of infection induced by rectal injections, found that the primary lesion took the form of necrosis of the superficial epithelium of the intestine, and concluded that the lesions are produced by cytolysis He thought that mechanical penetration of the tissues by the entamœbæ had no physiological effect as far as the production of lesions was concerned, but that bacteria play an important part, especially as secondary invaders Natural healing of the lesions in the cat apparently does not take place Amœbic abscess of the liver can arise in cats as early as four days after the appearance of dysenteric symptoms, in others as late as two or three weeks after

Experimental amœbiasis in the dog is a much more chronic disease S T Darling described a case of spontaneous amœbiasis in a dog and found that the whole colon was the seat of minute punctiform red erosions of the mucosa, covered with flakes of mucus The amœbæ had also produced ulceration of the ileum

The exact part played by the *E histolytica* in the production of the micro [illegible]

submucosa, where they produced flask-shaped ulcers

It is doubtful whether experimental amœbiasis has been produced in the rabbit or guinea pig, but, according to D L Martin, rats occasionally seem to be susceptible Natural amœbic infections are rare in animals (*see* Appendix) though monkeys in captivity contract it readily U Mello [illegible]

SYMPTOMATOLOGY OF AMŒBIC DYSENTERY

Like other protozoal diseases in man, amœbic dysentery exhibits the most varied clinical pictures Although acute and rapidly fatal cases undoubtedly do occur, yet they must be considered exceptional It has

already been pointed out that, on the whole, *Entamœba histolytica* endeavours to subsist on the best terms with its human host; therefore amœbic infection in man results, as a rule, in a long-drawn-out chronic disease Even when symptoms of dysentery are obvious, infection is compatible with fairly good health Cases are not uncommon in whic[illegible]
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of weight. W. [illegible]
amœbiasis as follows: "Like other protozoal infections, that of amœbiasis follows a protean course It may be fatal in a short time. It may become chronic with alternating periods of dysentery and constipation, or with passage of unformed stools It may be mild and cause little discomfort." So extremely variable are the symptoms of this infection that it may simulate almost any gastro-intestinal trouble. In chronic amœbic dysentery emaciation is the exception rather than the rule, but it occurs usually in the acute stage When death occurs it is the result of an accident, for example, of perforation of an amœbic ulcer with resulting general peritonitis; or of the opening up of some large blood-vessel in the intestinal coat, death then being due to uncontrollable hæmorrhage.

It is difficult to define the position of carriers in the symptomatology of the disease It has been pointed out that, if they are closely watched and studied over a period of years, some variations from normal health may be detected, and it is probable that, if they could be observed throughout life, they would be found to suffer periodically from mild dysenteric symptoms Furthermore, it is urged that there is the ever-present liability to hepatic amœbiasis (*see* p. 201), but, most important of all, they do constitute a potential source of danger to others.

It is possible to divide sufferers from primary intestinal amœbiasis

experimented with twenty volunteers by feeding them with amœbic

ysentery
In the
iated at
7–15 days, even up to 74–77 days, symptoms occasionally appeared within one week, and in a few cases not for three or four months

Duration of infection—Intestinal amœbiasis is undoubtedly one of the most persistent of all protozoal infections, it is probable that a

person, when once heavily infected, remains so for life, unless treated In the author's series of cases, in four patients the symptoms had persisted for twenty and, in one, for thirty years. C Dobell and A C Stevenson (1918) concluded that infection might persist for sixteen to thirty-four years Until recently it was comparatively common to find in England, uncured, ex-soldiers who had become infected during military service in India in the frontier wars of the last century, infections dating from the South African War of 1899–1901 were also encountered The author has recorded one case in a British officer who developed an acute attack of amœbic dysentery, which responded successfully to treatment, after he had resided seventeen years in England without experiencing any symptoms of this disease. A case of amœbic ulceration of the rectum has also been seen in an ex-soldier in whom symptoms of bleeding were first noted in 1937, i e, twenty years after he had contracted dysentery on the Somme in 1917 Furthermore, the symptoms of amœbic dysentery may vanish temporarily with apparent restoration of health, and these quiescent periods may last for two or three years The author treated, in 1937, an ex-soldier from India who suffered from an acute exacerbation of dysentery after a quiescent period of eight years, and in 1941 an erstwhile official of the Indian Forest Service who suffered from a recrudescence of amœbic dysentery thirty-one years after abscess of the liver

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diagnosis, from simple indigestion to cancer, is compatible with the very varied symptomatology of intestinal amœbiasis

The onset is seldom sudden, most usually it is gradual and progressive, and the patient, although inconvenienced, endeavours to carry on his work Very often it commences as a mild *diarrhœa*, and it is not until this has lasted several days that blood and mucus appear in the stool There is a large class of cases which may be labelled "amœbic diarrhœa," because, in the whole course of the illness, none of the more familiar symptoms of dysentery make their appearance A feature of the diarrhœa in amœbic dysentery, one it has in common with other serious abdominal diseases, notably carcinoma, is the alternation of diarrhœa and constipation Intense abdominal symptoms, such as excruciating pain, colic and tenesmus, which characterize bacillary disease, are generally absent There is usually consider- [illegible]
uld [illegible]
om- [illegible]
to bacillary dysentery, tenesmus is rare and was noted only in 7 out of the author's 535 cases.

Fever, as a rule, is not a feature of the amœbic, as it is of the bacillary

form of dysentery, except in the presence of some complication such as hepatitis. Exceptional cases with hectic fever have, it is true, been observed from time to time, but these are probably due to septic absorption from the extensive intestinal ulceration.

The author has records of mild pyrexia associated with intestinal amœbiasis in 10 per cent of his cases (1929). Pyrexia is naturally rare but can exist without any involvement of the liver. Occasionally the pyrexia may resemble a malarial attack, and when associated with rigors is probably an instance of periodic invasion of the liver by amœbæ derived from the bowel. (*See under* Amœbic hepatitis.)

[illegible]

treatment is peculiarly striking

The author has described one case of "amœbic fever" with hectic fever, persisting for sixteen days and of a remittent type which in its clinical features resembled typhoid

A seaman on arrival from Sierra Leone (July, 1940) had been ill with remittent pyrexia (104° F.), headache, bone-pains and signs of toxæmia. Meteorism was prominent, latterly, slight diarrhœa had been noted. On one occasion some blood and mucus were seen, but no amœbæ were found. Sigmoidoscopy revealed extensive ulceration, and in scrape preparations *E histolytica* were numerous Response to treatment was dramatic

It must be remembered that acute cases in the Chicago epidemic of 1933 presented rather unusual features. Many had an acute onset, [illegible] to such a degree as

liver abscess

The *stools* in amœbic dysentery are more copious than those of the [illegible] h fewer
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In acute amœbic dysentery *emaciation* occurs to a certain degree. In 43 out of 150 cases studied by the author (1929), the loss

of weight recorded was from fourteen to twenty-eight pounds in a year, and the greatest loss was of forty-two in three months. On the other hand, chronic intestinal amœbiasis interferes so little with nutrition that the body-weight is usually well preserved, and there are records of three cases in which a great increase of weight occurred. Intestinal amœbiasis is thus not incompatible with obesity.

Pain.—In intestinal amœbiasis subjective pain is, as a rule, localized [illegible]

[illegible] and perforation of that organ has occasionally been reported (p. 164) Moreover, experience shows that an appendicitis of septic origin may co-exist with intestinal amœbiasis (in the author's series (1941) in 5·4 per cent.)

[illegible]

border of the right rectus muscle, it may suggest cholecystitis On the other hand, there is a group of cases where colon pain is referred to the lumbar region, suggesting a misdiagnosis of pyelitis or renal calculus

Bowel symptoms.—In 114 out of 150 cases in the author's series (1929) chronic and painless diarrhœa was obvious without blood and mucus in the stool. On the other hand, the anomalous fact emerges that amœbic dysentery is compatible with constipation. Records of not less than eleven such cases have been obtained, and it has been shown that the cure for the constipation in these cases lay in the cure of the amœbic infection.

Flatulence. [illegible]

persistent that the disease may simulate chronic pancreatitis, chronic intestinal obstruction, or, indeed, sprue.

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total mortality rate was 7 per cent., and 3.9 per cent. developed liver abscess

The *stools* in amœbic dysentery are more copious than those of the bacillary form, are nearly always fæculent, and are usually much fewer in number, seldom exceeding twelve in the twenty-four hours; more usually they number three or four. They contain much dark and altered blood and have an offensive odour. Usually blood-streaked

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In acute amœbic dysentery *emaciation* occurs to a certain degree. In 43 out of 150 cases *studied by the author (1929), the loss*

Chinese, primarily regarded as epithelioma of the anus, for which colostomy had been performed before the discovery of *E. histolytica* cysts The inguinal glands were enlarged and hard Response to emetine injections and quinoxyl retention enemata was immediate

—These ulcers, which
and excavated, with
ical characteristics a
be ascertained by
and they yield most
satisfactorily to emetine bismuth iodide treatment The author has seen two such cases, both in ex-soldiers In the first, amœbiasis was contracted in France in 1917 and urgent symptoms noted 20 years later, the second was contracted in India and had lasted 10 years

Fulminating amœbic dysentery —These cases are rare Massive destruction of the intestinal mucosa, such as occurs in artificially infected kittens, may take place in man, when the patient succumbs to secondary *Bacillus coli* septicæmia

Fulminating cases were commonly observed

together with the most extensive ulceration of the whole of the large intestine, and massive infection of the blood stream with *Bacillus coli*

COMPLICATIONS AND SEQUELÆ OF AMŒBIC DYSENTERY

Accidental complications include *perforation* of an amœbic ulcer (usually in the region of the cæcum) and consequent general peritonitis This is nearly always fatal The author has had experience of four such cases

Hæmorrhage from a perforated artery in the base of an ulcer is another possibility

Stricture of the rectum does not commonly result (see p 18)

Dyspepsia.—Acute dyspepsia, which must be recognized as a feature of amœbiasis, may be the result of flatulence or may represent a reflex pain from the bowel. There is also the possibility that intestinal amœbiasis may be mistaken for duodenal ulcer This is a condition which rarely arises, but one case was so remarkable that a few details must be given.

history of amœbic dysentery of two years' duration. *E histolytica* in the active state were present in the fæces and were also demonstrated in scrapings from the rectum After treatment with emetine-bismuthous iodide, he recovered. Four years afterwards he was re-admitted with a palpable tumour in the left iliac fossa, which varied in size from day to day Barium enema showed a long filling defect (3½ to 4 in) situated in the descending colon immediately distal to the splenic flexure. At operation a large inflammatory mass (pericolic abscess) was found involving the splenic angle and descending colon and extending backwards to the vertebral column Removal of the mass was unjustifiable and, in fact, impossible, and a lateral anastomosis was performed between the transverse and sigmoid colons Recovery was uneventful (Plate VIII, p. 155)

Hæmorrhoids.—External piles are a very frequent accompaniment of intestinal amœbiasis Almost every case of long standing shows

somewhat purple colour

Spasticity of the sigmoid colon.—Spasm of the large bowel occurs in amœbic dysentery, especially in longstanding cases, and in those in which periodical constipation is a feature Spasmodic contraction may predominate over other symptoms and be ascertainable by abdominal palpation

Amœbic ulceration of the appendix—Amœbic disease of the appendix is by no means common, though chronic inflammatory appendicitis as a sequel to intestinal amœbiasis is not unusual In the author's series of seventy-three cases of appendicitis from the tropics coming to operation, fifteen had a definite previous history of intestinal amœbiasis, nineteen of bacillary dysentery, two of sprue W E Musgrave (1910) reported three deaths from perforative ulceration of the appendix in intestinal amœbiasis. Usually the causative organism is a streptococcus, or *B coli*, which may be associated with amœbic invasion of the bowel

E P Hogan (1920) gave a detailed description of such a case studied both

numerous entamœbæ were demonstrated on microscopic section

Sprue is a disease which appears to have some connection with amœbiasis Not *only is a double infection* of sprue and amœbic dysentery comparatively common, but also the former frequently supervenes upon the latter. In 32 per cent. of sprue cases it is possible to obtain a past history of intestinal amœbiasis (*see* p. 338)

Cachexia.—*There exists an ill-defined class of case in which* a condition of chronic ill-health exists without any outstanding obvious signs or symptoms These cases are best termed " amœbic cachexia," and increased experience of amœbiasis indicates that they are more [illegible]

[illegible] capacity is limited, and fatigue is evident in greater or lesser degree. *From physical examination there is little diagnostic guide, but the* stools may be found to contain *E. histolytica* cysts. Improvement in the general condition of the patient and his appearance after eradication of the infection is striking.

The most pronounced in the author's series occurred in a man of forty-six years of age, seen in 1931. The main symptoms were cachexia and [illegible]

The fæces were found to be heavily infected with *E histolytica* cysts. A remarkable change from his sallow, earthy complexion to that of health took place after a course of anti-amœbic treatment

Prolapse of the rectum.—*Rectal prolapse is brought on* by continual straining at stool, it may be the only outstanding sign of the disease, and becomes reduced when the patient is cured of his amœbic infection

[illegible] fæces revealed a massive infection with *E histolytica*, precystic forms, and cysts After adequate treatment the prolapse receded and the piles disappeared He has since been in good health

[illegible]

In the Hospital for Tropical Diseases, London, one case occurred of undoubted amœbic origin, which was successfully operated upon by Mr C. N. Morgan, and I am indebted to my colleague, Dr Carmichael Low, for his permission to refer to this case. The patient was admitted in 1930 with a

Cicatrization and stricture of the colon or rectum.—Contrary to assertions, stricture of the bowel due to amœbic ulceration is extremely rare One case with pericolitis, which was relieved by colostomy, has already been referred to (p 166), but this is the only authentic instance which has come under the author's notice, while Sir L. Rogers, who has examined over five thousand specimens in the Calcutta Museum, has recorded that he has never seen a genuine stricture.

Neurasthenia.—C F Craig (1929) has made a study of "latent" amœbic infection, the symptoms of which are confined chiefly to the digestive and nervous systems, and he describes certain definite *neurasthenic manifestations*. That the form found commonly in the tropics or "tropical neurasthenia" is frequently associated with chronic amœbiasis, nobody with a prolonged clinical experience can deny

Other sequelæ.—Chronic diseases of the intestinal tract which seem especially apt to follow in the wake of intestinal amœbiasis

but that they may legitimately be regarded as legacies of amœbic infection He has been under this impression for many years, and on *a reference to the records at the Hospital for Tropical Diseases the*

amœbic and three had a history of bacillary dysentery.

On the other hand, there are singularly few records of gastric ulcer in old dysenteric patients. Out of twelve proven cases, two had had intestinal amœbiasis and three bacillary dysentery.

There were twelve records of post-dysenteric dyspepsia, of which six occurred subsequent to amœbic dysentery · one of them had achylia gastrica, the other hypochlorhydria.

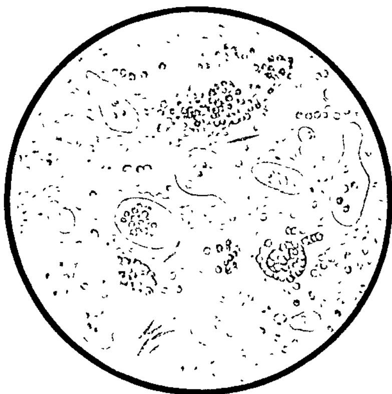
In seventeen cases of diverticulitis which were investigated no association with previous amœbiasis was forthcoming.

Carcinoma —J G Willmore* has shown that carcinomatous changes may take place in longstanding amœbic ulcers, and he has traced the history of nine instances of malignant disease of the colon developing in amœbic patients. In one he observed an amœbic ulcer, and was able to recover *E histolytica* in scrapings, but on re-examination six weeks after, a malignant growth was found at the same situation

The author has also encountered two cases of carcinoma of the rectum in association with subacute intestinal amœbiasis. It has been a common experience to find a carcinoma of the rectum or sigmoid colon in elderly patients suspected of dysentery.

A C Reed and H. H. Anderson (1936) investigated four cases of chronic amœbiasis in which carcinoma of the colon followed and accompanied the amœbic infection. They concluded that amœbic lesions may produce carcinomatous changes in two ways—by chronic irritation and by the production of benign adenomata which later become malignant. In three the new growth was situated in the sigmoid and in one in the cæcum.

* Personal communication



J H Mans n Bahr del

MICROSCOPIC APPEARANCE OF EXUDATE IN AMŒBIC DYSENTERY

Fresh preparation. Shows active Entamœba histolytica Some with ingested red blood-corpuscles, acicular Charcot-Leyden crystals and disintegrated intestinal epithelium.

PLATE IX

CHAPTER XII

AMŒBIASIS (*continued*): DIAGNOSIS OF AMŒBIC DYSENTERY

Microscopic examination of fæces.—To render the diagnosis of intestinal amœbiasis absolutely certain, it is necessary to demonstrate the *Entamœba histolytica* free or encysted It must not be thought, however, that a single microscopical examination will suffice; so varied and almost bewildering are the morphological phases of this parasite, that the examination should be performed by one who has long made himself familiar with it. For not only have the varying appearances of the amœba to be considered, but also its differentiation from other parasitic protozoa which may inhabit the human intestine, and from

are found in the fæcal contents during the chronic stage, and are never encountered in a blood-and-mucus stool.

Moreover, the various stages of *E. histolytica* found in the stools may afford valuable diagnostic data. For instance, the carrier of *E. histolytica* passes normal stools containing cysts but no active amœbæ If purged, he probably passes amœbæ, very rarely large, tissue-invading forms containing red blood-corpuscles. In the acute stage, however, nearly all amœbæ are of the tissue-invading type. In liver abscess, the amœbæ in the pus are tissue-invading forms; cysts or precystic amœbæ are never produced. On the other hand, it is exceptional to find tissue-invading forms in chronic amœbic dysentery

Difficulties connected with the microscopic diagnosis of amœbic dysentery must be emphasized. The portion of the stool most likely to reveal organisms is one which contains mucus streaked with blood,

most
buted
them
times
bowel

surface when examination has proved negative In those patients with secondary amœbiasis, such as liver abscess, the fæces may contain no evidence of amœbic infection.

In the chronic stage it is often difficult to find cysts. For some reason, they may appear in large numbers once, then disappear even when conditions appear favourable; it is, therefore, necessary to

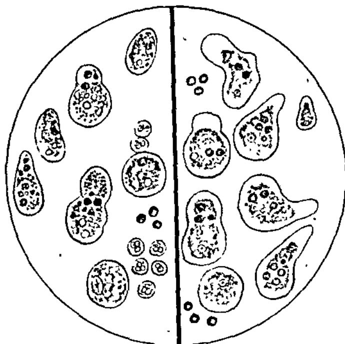


Fig. 22 —Diagram showing differentiation of *E histolytica* from tissue cells.

Left, macrophage cells and pus cells in exudate of bacillary dysentery, with ingested red blood-corpuscles. Right, *Entamœba histolytica*, active and precystic forms, in amœbic dysentery stool.

examine specimens on six or more consecutive days before establishing a negative diagnosis. Under these circumstances it is more likely that amœbæ and cysts will be found if the patient is freely purged with a saline. Castor oil and oily medicaments must be avoided, for the droplets so produced render it impossible to examine the stools with any degree of accuracy E. Reichenow (1926), however, who made daily observations on his own excreta for six months, found, by counting the cysts, that they diminished in numbers after a saline purge. P. Ravaut

result from cytolysis of eosinophil cells or may be an excretory product of the amœba

We may conclude that Charcot Leyden crystals are not necessarily diagnostic of amœbic dysentery, but may constitute a useful indication.

The sigmoidoscope as an aid to diagnosis.—Lesions of amœbic dysentery occur in the rectum and the sigmoid in over 80 per cent. of the cases of this disease and extend down to the internal sphincter As seen in the living subject, these lesions are quite distinctive, but differ considerably in appearance from the grosser lesions seen in pathological specimens. After death, the more superficial and dis-



Fig. 23 —Chronic amœbic dysentery . fæces preparation showing two cysts of *Entamœba histolytica* and one of *Entamœba coli* (unstained)

tinctive details disappear and many of the delicate tints which characterize the living ulcers are lost Moreover, some lesions are so

more diameters It is not possible to diagnose every case of intestinal amœbiasis by means of the sigmoidoscope, because in a certain proportion lesions are confined to the cæcum and ascending colon, far beyond visible range.

Not only can the character of amœbic lesions be recognized by sigmoidoscopy, but amœbæ may be demonstrated in scrapings taken

and G Krolunitski (1916) advocated intravenous injection of 1–4 cgm of mercuric cyanide which, they state, increases their numbers.

It is hardly necessary to emphasize that, for successful microscopic diagnosis, the fæces must be fresh, especially in the acute stages, for amœbæ degenerate and die rapidly outside the body, usually within two hours The cysts, on the other hand, being designed by nature for external life outside the body, remain alive and recognizable in the stools for days—even for several weeks—under ordinary conditions If a few drops of formalin be added, the cysts in the fæces will retain characteristics almost indefinitely.

Where cysts are scanty, repeated examinations increase the chances of detection; thus D L. Mackinnon recorded that after six examinations the percentage of positive findings is increased eightfold. In 1,680 fæces examined on one occasion only the percentage of positive findings was 4.3, but after six examinations it increased to 34 6.

W. M. James (1927), working with fresh material, and with permanent preparations, *has been led to believe that in trained hands positive* results can be expected at the first examination in 75 per cent. of cases, but at a second the percentage is increased to 90. Should a third examination not disclose a *histolytica* infection, positive results need not be expected.

At the Hospital for Tropical Diseases, London, the three-stool examination test is adopted as a routine. It has proved to be the [illegible] an occasional case [illegible] eries of 535 proven [illegible] *tolytica* were found [illegible] ystic forms, in 287, and *E histolytica* in scrapings from rectal ulcers, but not in fæces, in 26.

Technique of microscopical examination.—This subject is fully dealt with in the Appendix (p 551). It is only necessary to emphasize that the stools should be as fresh as possible, and when they contain blood and mucus a portion of this should be selected for microscopical examination. A warm stage is not necessary if the stools are freshly passed and are kept at body temperature in a warm room. As N. D. [illegible]

J. G. Thomson and A. Robertson (1921), who paid attention to the presence of Charcot-Leyden crystals in amœbic dysentery stools, found them in 25 per cent of *proven cases of intestinal amœbiasis* They are most common in [illegible]

by the accumulation of inflammatory tissue at the base, so that it projects above the ulcer margin and presents itself as a greyish-white covering, known as the "white-cap," over the centre of the ulcer. This white-cap is swabbed away, and the true base of the ulcer is

glass slide and covered with a few drops of physiological saline solution, but in the author's experience this method usually produces too much bleeding to be of any practical value

Subacute stage.—Here the bowel presents the same rugged folded appearance, but much blood-stained mucus is usually present in the

e form of the minute yellow
ribed, and various stages may
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membrane with hæmorrhagic

the mucosa may be present, or definite deep ulcerations may be visible, with undermined edges, hæmorrhagic margins, and yellowish or grey-coloured bases. (Plate V, D, facing p. 78.)

Solitary rectal amœbic ulcer —On rare occasions a large ulcer, 1–2 cm in diameter, is seen inside the anal margin, and may give rise to considerable pain and bleeding The author has encountered cases which were suspected of being malignant in origin, but which on scraping proved to be due to the *E histolytica* It is important, therefore, that any ulcer of the bowel in a patient coming from an endemic zone of the disease, should be examined from this viewpoint (Plate V, C, facing p 78)

A case of indurated ulcer of the rectum, which on digital examination gave the impression of malignancy, occurred in the author's practice *E histolytica* were demonstrated in scrapings from an ulcer 9 cm. from the anus, and other lesions were subsequently found at a higher level in the rectum and sigmoid The patient had, apparently, been originally infected

from lesions by a special spoon (*see* p. 10). The edge must not be so sharp as to destroy the lesions and cause hæmorrhage, nor yet too blunt to remove sufficient tissue for examination. Difficulty may be experienced in transferring the small amount of material from the hollow of the spoon; a porcupine quill forms the best instrument for this purpose. The material thus obtained is suspended in saline, covered with a slip, and examined without delay. Sometimes it is difficult to obtain sufficient material in the hollow of the spoon, and it is then better to scrape the exudate into the sigmoidoscope. The author's statistics are based upon 535 cases of amœbic dysentery definitely diagnosed in the years 1920–39. Of these, 509 were diagnosed by microscopical examination of the fæces; sigmoidoscopic examinations were made in 258 and lesions demonstrated in 234. In 77 *E. histolytica* was found in scrapings; in 24 (9 3 per cent.) the mucosa appeared normal The author has also shown that cysts of *E histolytica* are usually more numerous, and therefore more easily detected, in the fæces which are adherent to the mucosa and removed through the sigmoidoscope.

Acute stage.—The distinctive characteristics of amœbic lesions, as compared with those of bacillary infection are their superficiality, the comparative painlessness with which the examination can be carried out, and the laxity and elasticity of the mucous membrane. The ulcers are scattered so that the intervening mucous membrane remains normal. Individual ulcers are small—only a few millimetres in diameter —*and never, in the author's experience, resemble the large, undermined, oval-shaped ulcers so often encountered post mortem.* In

The earliest amœbic lesions in the rectum consist of small yellow elevations with a hyperæmic margin, which mark the site of future ulcers. In association with these elevations, fully developed amœbic

amœbiasis. When scrapings are made from the hæmorrhagic surface, amœbæ may sometimes be demonstrated. This surface infection resembles the intense condition produced in experimental amœbiasis in kittens. These lesions usually extend down the rectum to the *internal sphincter* and occasionally to the anal margin.

In America W C. Boeck and W. D. Smith, G. S. Gant, and L A Buie have devoted attention to amœbic lesions as seen by the sigmoido-

Complement-fixation and other serological tests.—C. F. Craig in his most recent publication stresses the value of this test

Craig has now published the results obtained in 1,000 cases, in which the findings were checked by an examination of the fæces for *E histolytica*; 17.5 per cent gave a positive result and 82 5 per cent a negative one Of the 175 persons giving a positive reaction, *E. histolytica* was found in the fæces of 157, or 89.7 per cent. On the other hand *E. histolytica* was found in the fæces of 1.4 per cent. of the

returned in 92 per cent, and reports failed to agree in 16 7 per cent It is evident that considerable improvement in the preparation of antigen is necessary before this test can be relied upon.

In studying precipitins in cats infected with *E histolytica*, E H. Wagener in [illegible] prepared test antigens by [illegible] scrapings of [illegible]

were obtained.

Intradermal tests.—As aids to diagnosis attempts have been made to elaborate an intradermal test, such as that of L. Scalas (1923). The test material
fragments of the
amœbic dysentery
incubating for a
and finally decolo
the injection of 0 25 c c intradermally was followed in an hour by swelling and redness accompanied by itching and a sense of heat. These signs disappeared in one to three days As the results were somewhat indefinite, it is essential that these experiments should be repeated, using a test material containing a higher concentration of amœbic substance, possibly from cultures

in this viscus, but similar appearances are seen in forms of dysentery and colitis unconnected with *E histolytica*.

in France in 1917, and it had taken twenty years for symptoms of rectal bleeding to develop. This large indurated ulcer granulated up within seven days from the commencement of emetine-bismuth-iodide treatment, and three weeks later had epithelialized; within a month no traces of the former ulcer could be seen. A second case—an Indian infection of ten years' duration—was subsequently recognized.

of the disease for a period as long as five, six, or even seven years. It is, therefore, important that some distinctive appearances of the bowel surface should be recognizable. Lesions in these latent cases *often take the form of small yellow papules, or the whole surface* of the rectum may be studded with microscopic depressions or pits (a pock-marked appearance) which represent healed ulcerations, but may be difficult to detect

Carrier state.—Interest especially centres in lesions which can be seen in those who are carriers or "cyst-passers" of the amœbæ, that is to say, persons who, although showing no symptoms or signs of dysentery, yet continue to pass cysts of *E. histolytica* in their fæces By sigmoidoscopy the bowel usually appears normal, but sometimes granular patches or small scattered hæmorrhages alone indicate the site of minute amœbic ulcers

The sigmoidoscope as a guide to treatment.—The lesions in various

Within twelve days from the commencement of the treatment, epithelialization has already taken place, and in a short time it becomes difficult to recognize the site of the former ulcers In a healed bowel active signs of amœbic infection are absent, though small depressions or pits stud the mucosa and remain visible for years

The blood count as an aid to diagnosis.—In acute cases of intestinal amœbiasis the average red-cell count varies between four and

should arouse suspicions of a possible liver abscess. The author,

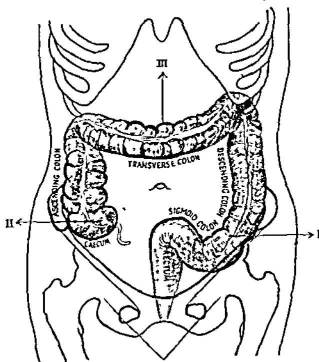
present In chronic cases, however, there is no leucocytosis, but a relative decrease of the polymorphonuclears to 57 per cent and a slight increase of the lymphocytes to 34 per cent. As a working rule, the leucocyte count is higher in intestinal amœbiasis than in bacillary dysentery.

and striking "cone-like" deformity of the ileo-cæcal valve, as well as a deformity of the lower end of the cæcum

G. Mather Cordiner* reports on radiographs of more than 150 cases of proven amœbiasis by the opaque enema. In only two has he observed deformity of the cæcum with incompetence of the ileo-cæcal valve comparable to that described by J C Bell In one case this deformity was proved to be inconstant In non-amœbic cases six were similar In his opinion it is possible to assume the existence of colitis, but not the specific nature of the lesion.

Differential diagnosis of intestinal amœbiasis from diverticulitis, ulcerative colitis, bacillary dysentery, mucous colitis, intestinal bilharziasis, polyposis, and other forms of intestinal disease is fully dealt with in the sections which treat of these conditions (Fig 24)

* Private communication



P. H. M.-B.

Fig. 24.—Diagram illustrating diagnostic points in the clinical diagnosis *of amœbic dysentery.*

The arrows mark the position of deep tenderness on palpation. I, amœbic focal point, on pressure of the first portion of the sigmoid against the pelvic brim. This is present also, sometimes, in chronic ulcerative colitis, and in chronic bacillary dysentery; II may be found alone or in association with I, III, giving rise to epigastric tenderness, may cause confusion with gastric or biliary disease. The heavily-outlined portions indicate the areas of amœbic infiltration which can be elicited on deep palpation Grosser degrees of infiltration are found at I and II in diverticulitis, and at II in Crohn's disease, in intestinal bilharziasis, and also in tuberculosis of the cæcum.

' valve,
om the
e same

emetine after being subjected to its action Thus A Halawani (1930) has demonstrated an increased resistance by amœbæ in culture [illegible]

Emetine in tablet form by the mouth has proved useless as it provokes emesis

Method of administration —There has been much discussion on [illegible]

tissue, are much better tolerated and much less painful When emetine is injected into the muscular tissues every care must be taken to eliminate any source of focal sepsis first, or a fixation abscess may occur at the site of the injection The author had an alarming experience of this, when, in one of his recent cases, a large gluteal staphylococcal abscess formed at the site of injection, a metastasis from a septic prostatic abscess

Intravenous injection does not find many advocates at the present time The drug is much too toxic, and is especially likely to act upon the heart

It is generally agreed that emetine is the most useful drug in the early stages of hepatic amœbiasis, in this condition subcutaneous and intramuscular injections are followed by the best results

[illegible] exercise

The action of emetine on *E. histolytica* in the stools is very rapid In 1922 the author [illegible] amœbæ had disappeared

The action of emetine has been studied by W M James (1913) He discovered that changes in the cytoplasm of the amœbæ in the fæces occur after an initial dose of one-sixth of a grain of emetine, after [illegible] over 12 stone (76 2 [illegible] for the first three [illegible] be continued To children of eight years of age, half a grain should be administered and to still younger ones, one-sixth (According to A C Reed the

CHAPTER XIII

AMŒBIASIS (*continued*): THE TREATMENT OF AMŒBIC DYSENTERY

THE treatment of intestinal amœbiasis is a problem to which much

restoration of damaged tissues.

If it is permissible to crystallize the results of experience in an epigrammatic statement, it may be said that the more acute the attack of amœbiasis and the more striking the symptoms, the more *dramatic the cure and the more permanent the results.*

Ipecacuanha.—Ipecacuanha is the powdered root of a rubiaceous

and N. C. Macnan advocated it as

but their observations were largely forgotten in subsequent decades

The ipecacuanha root contains at least four alkaloids, of which the most important are emetine, cephaëlin, psychotrin, and methylpsychotrin. The two toxic substances are emetine and cephaëlin, which may cause gastro-intestinal symptoms, nausea, vomiting, and diarrhœa, but which are specific for *E histolytica.*

Emetine. *History.*—Emetine was isolated from ipecacuanha by Pelletier

d and E H. Wagener, in a dilution of one in

a million, by ... last observer found

that the drug acts best in an alkaline medium

three months' treatment with massage and electricity, muscular function was once more fully restored

W. A. Young and G. R Tudhope (1926), from their experimental work, consider that the action of emetine is concentrated upon the muscle-fibres rather than upon nerve-endings

The effect of emetine upon the cardiac muscle is a subject which has attracted the attention of pharmacologists, and to which too little attention has been paid by the practitioner in the tropics. R N Chopra and B Sen found that the systolic blood-pressure falls to 90 and 100 mm. after emetine therapy, and tachycardia of sinus origin—even auricular fibrillation—results Lethal and sub-lethal doses cause severe injury to the myocardium in rabbits, but some time elapses before the morphological changes become apparent; when given in large doses the heart-beats are slowed, weakened, and fade away. Auricular fibrillation may precede heart failure, while with increasing doses, respiratory paralysis may be produced.

When giving emetine in pregnancy and after parturition, it should be remembered that it has an effect upon the uterus, as has been demonstrated by D Epstein in cats

In minor degrees of emetine intoxication the patient complains of weakness of the calf muscles, often associated with numbness and paræsthesia of the soles Very commonly after a course of emetine-bismuth-iodide stiffness persists in the legs for a considerable period.

The author has notes of four cases of emetine intoxication in which the [illegible] other cases extreme weakness of the muscles was the cardinal feature, with loss of reflexes In one man of fifty three who had received 16 grains of emetine bismuth-iodide, both arms and legs were affected In 1929 the author saw a man of forty four who had paresis of both legs with loss of deep reflexes, atrophic skin and brittleness of nails following upon emetine injections which had been given continuously over a period of two months

Although emetine is the most efficacious drug in the acute stage, yet the author contends that only rarely does it entirely eliminate the infection, so that an after-course of emetine-bismuth-iodide is necessary

The widely-practised procedure of periodic injection of emetine is, in the author's experience, to be deprecated, as it merely tends to render *E histolytica* emetine-resistant. These clinical observations receive support from the laboratory experiments of H Bonnin and R. Aretas (1939) who, by exposing *E histolytica* in cultures to increasing concentrations of emetine, found it was possible to produce strains resistant to this drug

Emetine bismuthous iodide (*Emetinæ et bismuthi iodidum*, B.P., 1932) (E B I).—The combined iodide of emetine and bismuth is prepared

total amount of emetine in one course should not exceed 0.01 gramme per kilo body-weight.)

In addition to emetine injections, Rogers originally advocated the administration of ½- to 1-grain doses of emetine by the mouth, presumably given in keratin-coated capsules, or the combination of emetine injections with powdered ipecacuanha, 20–30 grains. The object of this mass attack is to destroy *E. histolytica* while still in the active and vulnerable stage.

Emetine by enema.—Attempts have been made by the author to introduce emetine directly into the bowel. This causes a considerable amount of pain and is by no means successful. Even when given in a dilution of 1 : 1,000 (4 grains in 10 ounces of normal saline) violent spasms were produced, and parasitic relapse with blood and mucus in the stools ensued.

Results.—Experience has shown that, though the immediate therapeutic effects of emetine are most striking, this drug alone does [illegible] ious solely [illegible] ut has no

In eighty-seven cases investigated by the author in London, 1920–2, more than half (forty-eight) had sustained a relapse. These patients contracted their infection during war service and gave a subsequent history of relapses over a period of four to six years. All had received prolonged treatment with emetine injections, two having been given as *much as 70 grains consecutively, and one as much as 120 grains*, the average in most cases being 8–16 grains.

[illegible]

therapy complains of mental depression, weakness, and loss of sense of taste for food and tobacco; a fall of blood-pressure of 10 mm. or more of mercury can usually be registered. In extreme cases paresis of the legs, with toe- or foot-drop, loss of knee-jerks and some degree of paræsthesia have been encountered.

Occasionally emetine may attack one particular group of muscles, producing a condition resembling early progressive muscular atrophy. This is probably a true myositis, since the atrophy is preceded by myotatic irritability and muscular pains.

In June, 1920, the author was consulted by a doctor who was very sensitive to emetine. He had suffered for four years from recurrent attacks of amœbic [illegible]

(e g , 19 or 20 grains) are just as efficacious Results are equally

the drug It may then be taken with a small quantity of tea or water; a sedative, *tinct. opii*, 10 m , chloretone 10 gr , or luminal, 1 gr , should be administered half an hour previously The pillows should be removed, and the patient should be laid flat on his back and warned to remain perfectly quiet. Any saliva which has accumulated in the mouth should be expectorated. Vomiting may occur immediately

tolerance to further E.B I

Successful E B I treatment is followed by a diarrhœa in which the stools assume a dark brown or blackish coloration

All authorities who have written on this subject are agreed that, although remarkable recoveries take place by the proper use of E B I, yet in a large series of cases a certain proportion prove refractory, and there appears to be no object in persisting with this drug when once relapses have become established.

In a series of 134 cases the author has recorded ten relapses within a period of six weeks from the commencement of treatment, with a return of symptoms and the demonstration of amœbæ in the stools Three patients relapsed after as many as nine separate courses of E B I in which 30 grains or more had been given, and there are reasons for believing that a strain of emetine-resistant amœbæ had been produced

E B I is not so effect [illegible]

Treatment with E B I is a great advance upon the original emetine method, and some experiences can be quoted, of which the following is an example —

E B I in therapeutic doses has no effect upon any other species of amœba which parasitizes man, except *Iodamœba butschlii* (*see* p 534), nor has it any action upon other intestinal protozoa It is more toxic to monkeys than it

by precipitation from a solution of emetine hydrochloride by the addition of a solution of potassium-bismuth iodide. It contains not less than 25 per cent. and not more than 28 per cent. of emetine ($C_{29}H_{40}O_4N_2$) and not more than 18 per cent. of bismuth.

This drug was introduced for the treatment of chronic intestinal amœbiasis by A. G. Dumez in 1915, and its effects were first tested on man by H. H. Dale and by G. C. Low and C. Dobell in the following

It is sometimes put up in pills coated with keratin, but experience has frequently shown that they are apt to be passed unabsorbed in the stools. Probably salol-coated pills are more readily absorbed (D. G. Lillie and S. Shepheard)

In treating patients with E.B.I., it is necessary, to give the drug full effect, that the patient should be confined strictly to bed. In subacute and acute cases this is usually not difficult, but patients who *are chronic carriers without definite symptoms may object. Unless rest* is enforced, however, vomiting will almost certainly occur, and there may be diarrhœa, which almost invariably follows E.B.I., and the danger of heart trouble

d on

the

place

as the compound is spread over the surface of the intestines

Intensive E.B.I. treatment may be trying to the patient, for it is

(systolic). Subsequent experience has shown that it is not necessary to diet the patient so strictly (*See the* diet sheet, p. *169*.)

The best method is to give a preliminary aperient consisting of

* It appears that a case of dysentery was treated by Tull Walsh in India with the double iodide of emetine and mercury as long ago as 1891, with preparations which were advocated by Warden

combination with iodine (7-iodine-8-oxyquinoline-5-sulphonic acid). It contains 28 per cent. of iodine with sodium bicarbonate, and is a yellow powder exhibited in the form both of pills and of retention enemata. At first its use in dysentery was a pure experiment, but it now appears that it exerts a specific action upon the *E histolytica*, as shown in culture tests V. Nossina (1934) finds that the effective range is between pH 5 6 and 7 8 in a concentration of 1 . 5,000 P Muhlens and [illegible] undergone appendicostomy and cæcostomy. In both instances an almost immediate clinical improvement took place

It is probable that a satisfactory and permanent result cannot be obtained when this drug is administered by the mouth Quinoxyl pills contain 4 grains (0.25 grm), and it is recommended that as many as six should be given in a day In the author's experience this causes a considerable diarrhœa, is usually badly tolerated, and moreover fails to exterminate amœbic cysts If it is necessary to give it by the mouth, Muhlens has worked out the following scheme —

On the first day, three pills of 4 grains each (0 25 grammes) are given , from the second to the fifth day, two pills three times a day, if tolerated ; and on the sixth and seventh day, three pills three times a day The pills are best [illegible]

[illegible]

Soon after its introduction it became apparent that quinoxyl is [illegible]

The bowel should first be washed clear of mucus by an enema consisting of 1 pint of 2-per-cent sodium bicarbonate, which is best given at 8 a m. One hour later 200 c c. (8 oz.) of a 2 5-per-cent solution of quinoxyl in warm water is introduced [illegible]

is to man, but it apparently eradicates a *histolytica* infection in these animals. C. Dobell and A. Bishop (1921) treated five tame monkeys with E.B.I. by the mouth in order to study this effect. These monkeys were originally infected with *E. histolytica*, *E. coli*, *Endolimax nana*, *Enteromonas*, and *Giardia* It was necessary to administer 60 mgm. of E B I. daily for a week to a macaque weighing 5 kilos, in order to eradicate the infection; but this dose was toxic to four out of five animals.

Emetine does not, as a rule, cure acute amœbic dysentery in the cat, and it is pointed out that if this animal had been originally used to test the curative action of the ipecacuanha alkaloids, the therapeutic action of emetine in human amœbiasis would never have been discovered.

The modification of [illegible]
—was introduced by [illegible]
irritating than E B.I [illegible]
each containing 2 gr [illegible]
combined with tablets of ox bile, 5 grains, three times a day. It has been claimed that vomiting and other phenomena frequently associated with E.B.I. do not result with this compound.

The periodide of emetine contains 38.7 per cent. emetine and 61.3 per cent iodine Insoluble in water, it is readily soluble in alcohol, chloroform, ether, and other solvents. By analogy with other alkaloidal periodides, the alkaloid would split off from the other iodide [illegible]

the latter drug, it may be given at night, in doses of 2 grains, when E.B.I. is not well tolerated

Another compound, *auremetine* (Willmore and Martindale), a compound of auramine—an aniline dye—and emetine, was introduced in 1926 It is a dark maroon powder, insoluble in water, and is a combination of the hydriodide and periodides of emetine and auramine —emetine *28* per cent., auramine *16* per cent., and iodine *56* per cent. It was claimed that it did not give rise to nausea or vomiting, and could be tolerated in doses of 1 grain in gelatine capsules, four times daily. This, also, has not been found better than E.B I

Gavano (Bayer), a derivative of ipecacuanha—probably cephaëlin in [illegible]

six consecutive days.

Quinoxyl. *Chiniofon* (B P.), *Yatren*, *Dysentulin* (Germany), *Anayodin* (U.S.A.).—In 1921, P Muhlens and W. Menk introduced this substance for the treatment of chronic amœbic dysentery. Quinoxyl ($C_9H_6O_4SNI$) consists of oxyquinoline-sulphonic acid in

Scheme of Dietary and Combined Treatment for Intestinal Amœbiasis

On waking	Potassium chlorate mouth-wash.
7 a.m.	Tea and 2 oz milk.
7 30 a m	One egg, buttered toast, cup of tea and 2 oz milk
8 a.m.	Sodium bicarbonate enema (2 per cent)
8.30 a m	Quinoxyl ($2\frac{1}{2}$ per cent) by rectum (7 oz)
9 a m	8 oz. milk
10 30 a m	[illegible]
12 noon.	[illegible]
4 p m	[illegible]
5 p m	[illegible]
6 p.m.	Milk 8 oz., bath.
9 30 p m	Sedative (luminal gr. 1–gr $1\frac{1}{2}$, chloretone gr. 10, or nepenthe min 10).
10 p m	E B I. gr. 2.
10 30 p m	Sleep

At the termination of the treatment the patient should be permitted two days' respite in order to recover from the strain of active treatment and to regain his "sea legs," for nearly always a sense of weakness or stiffness results

Should a relapse of amœbic dysentery occur after this thorough treatment the course may be repeated, and the strength of the quinoxyl [illegible]

which the cases were drawn renders satisfactory follow-up impossible This, however, has been satisfactorily carried out and many have been periodically re-examined over a period extending from ten to fifteen years.

In the author's opinion this is the most efficacious form of treatment for intestinal amœbiasis yet devised At the same time it would be going too far to say that it *never* fails The main point is that the treatment must be conscientiously carried out with strict observance of detail

[illegible]

home to England In September [illegible]

derived from the bowel Ten such treatments are necessary on as many successive days

It is necessary to emphasize that quinoxyl should be given as a retention enema and *not* as a cleansing enema There is proof that quinoxyl introduced into the rectum percolates through the large intestine.

This was found in a patient who died suddenly from coronary thrombosis in February, 1929 He had taken, altogether, 27 grains of E B I without any untoward symptoms being provoked, and at the same time ten quinoxyl *retention enemata. At autopsy quinoxyl was found coating the mucosa of* the large intestine

Though well tolerated, quinoxyl is apt to provoke diarrhœa, but this can be controlled by strict diet and rest in bed That it exerts a direct

rosy rash results

Combined treatment.—Combined treatment consists of injecting quinoxyl into the bowel (retention enemata), and at the same time

the lower bowel

Experience has shown that it is unnecessary to give more than a

In order to *prevent emesis and nausea, 1 or 1½ grains of luminal should* be given half an hour before the E B I , occasionally two tablets of allonal, 10 minims *tinct opii* (nepenthe), or 10 grains of chloretone are

atment,

irritation. According to these observers the drug is more satisfactory than quinoxyl.

Rivanol, a derivative of acridine (2-æthoxy—6-9-diamino-acridine-lactate), was first recommended by O Urchs and F. M. Peter. It is given as an enema in 1 : 2,000 solution, 500–800 cm being injected at body-temperature, with the patient lying on his left side and afterwards adopting the knee elbow position Its action is said to be increased by the exhibition of sodium sulphate by the mouth The enema is retained as long as possible —for at least fifteen minutes—and it is said that a course of ten or more treatments are necessary This subject is dealt with by T Ronnefeldt (1931) and A G Biggam and M A Arafa (1930) Various opinions have been expressed [illegible]

by the mouth in doses from 30 to 50 milligrammes daily Children receive a tenth of this dose

Kurchi bark and its derivatives.—The alkaloid of kurchi bark, (*Holarrhena antidysenterica*), a small deciduous plant from the Himalayas, conessine, has been found to exert some action upon the *E histolytica* in vitro *Kurchine hydrochloride* (Whiffen & Co) is the crystallized alkaloid [illegible]

bismuthous iodide was introduced by H W Acton and R N Chopra (1933) [illegible]

permanent cures in cases of amœbiasis, treated by this method in India, who have returned to England

Stovarsol, acetarsol, or spirocid (acetyl-oxy-amino-phenyl-arsonic acid), was synthesized by Fourneau and introduced by E Marchoux (1922) for the treatment of amœbiasis in France It contains 27 2 per cent of organic arsenic Although it has definite value as an intestinal tonic and in the after-cure of amœbic dysentery, it cannot be said that the French claims to its value as a reliable amœbicide have been fully substantiated On account of its simplicity stovarsol has been extensively used in treating mild cases of amœbiasis and carriers, and, according to E F Craig, in his practice, 60 per cent of infections were eliminated after one course of treatment He has, however, had to abandon its use on account of its toxic propensities

It has been customary to exhibit this drug in doses of 4-grain tablets (0 25 gramme), twice daily for ten days, as an after-treatment, and in carriers who for various reasons cannot undertake vigorous courses of treatment It is necessary to emphasize that there may exist a definite

histolytica cysts were discovered in large numbers in the fæces Again he went through an *intensive course of treatment lasting nearly one month*, but in place of emetine injections he was given large doses of auremetine by mouth, combined with retention enemata of quinoxyl. In January, 1934, as the stools were still positive, several new preparations were tried. In May, 1934, as he was suffering from diarrhœa with constantly positive stools, he came to London for treatment and received the combined emetine-bismuth-iodide (19 grains) and quinoxyl retention enemata in double strength, after which he felt well and remained cyst free till the end of June. In July, they were again present in large numbers, but circumstances necessitated his return to Nyasaland with instructions to take monthly courses of a quinoxyl derivative

Two years afterwards, in July, 1936, he returned on leave and his stools were examined constantly, over a period of three weeks, with a negative result

F

cases

exhib

practically the same as quinoxyl. It is exhibited in the form of a pill of 4 grains, each pill containing 8 to 10 grains of sodium bicarbonate to increase the solubility, and 12 pills are given daily (i e , four after each meal) for eight days According to O'Connor no other form of treatment is necessary. *E. Tonnard-Neumann and F. Valera (1931) have compared the* actions of anayodin and quinoxyl and have been unable to distinguish any differences in therapeutic action between the two

Author's summary of ultimate results of treatment of 535 cases of amœbic dysentery (1941)

I Anti-amœbic treatment of 276 primary (previously untreated) cases.

E.B I, E.P.I, quinoxyl and quinoxyl retention enemata	57
Combined treatment	
E B.I, + quinoxyl retention enemata	219

Relapse rate, 1 4 per cent. Treatment repeated, all finally cured.

II. Treatment of 259 previously emetine-injected cases in addition to inadequate amounts of E B.I, E P.I, quinoxyl, stovarsol, or carbarsone.

E.B.I, E P I, 30–40 grs	100
Oral quinoxyl + retention enemata	17
Combined treatment	142
Relapse rate	7.7 per cent.

It is therefore contended that previous intensive emetine treatment renders the disease more difficult to eradicate

Bismuth subnitrate.—For many years W E Deeks (1914), in

before use It may be given by the mouth (but the taste is acrid), three teaspoonfuls a day or by means of an enema of 12 ounces Treatment should be continued for ten days

dosage

Kho-sam —This also is a native cure for dysentery Prepared from the seeds of *Brucea sumatrana* (*Simarubaceæ*), it has been recommended by French workers in Cochin-China, but there is no evidence that it contains any active principle

Uzara, of which the active principle is uzarine, is the name for a native remedy derived from an African plant of the family *Asclepiadaceæ*. It is given in the form of a tablet This drug appears also as a proprietary preparation—*Panzaron*—that has been recommended by German workers

Salvarsan has been recommended by French workers for refractory cases of intestinal amœbiasis, administered intravenously, orally, or rectally P Ravaut has recommended neosalvarsan injections combined with emetine, and it certainly does appear to be efficacious in those cases in which a history of syphilitic infection can be obtained

sugar and cream and eaten in small amounts with each feed of milk, or it may be given in an infusion in the form of bael fruit tea. It is an adjuvant to the treatment of amœbic dysentery

Ravaut's paste, introduced by P. Ravaut and Charpin in 1919, consists

idiosyncrasy to stovarsol. Its action on the Entamœba is due to the arsenic it contains, and cases of arsenical poisoning, sometimes even fatal, have followed. On no account should patients be allowed to take the drug without strict instructions regarding its possible toxic effects. Optic atrophy is possible from gross overdosage.

One of the most common forms of stovarsol poisoning consists of an urticaria-like rash on the face, neck, and trunk, together with pyrexia, and sometimes adenitis, it so closely resembles German measles that two cases in the author's practice were sent to a fever hospital, and other instances have been reported in the literature (F. D. Annesley, 1928) There is also a curious form of delayed stovarsol poisoning. H C ... otoms were i ... odium thiosu ... natitis (J Morgan, 1926)

combined with emetine therapy

Carbarsone ($H_2O_3As_2C_6H_4NHCONH_2$), as originally prepared by Ehrlich, is 4-carbamino-phenyl-arsonic-acid, containing 28.8 per cent ... In America

non-toxic in effective doses, and it may conveniently be administered *orally without interfering with the patient's usual mode of life.* Its therapeutic action is due to arsenic, and it is less toxic than stovarsol Nevertheless this drug should be administered only under supervision. (Recently a fatal case of arsenical poisoning has been reported after its use (*E Epstein, 1936*)) *The author's experiences of the end result* of carbarsone-treated amœbic dysentery have not been favourable. One such case may be quoted

treatment

Both stovarsol and carbarsone may be administered in the form of retention enemata of 2 grammes in 200 c c of warm sodium bicarbonate solution

Amibarson is a new compound with a chemical composition similar to carbarsone and with a similar action (*R N Chopra, B Sen and G Sen, 1935*)

bowels perfectly normal, no further symptoms. Increase in weight five pounds

(2) *Duration twenty-one years.*

Mrs E. W., 64, spent six weeks in Bombay and ten days in Colombo in 1913, never in tropics since Ever since has had chronic diarrhœa In 1929 had a liver abscess from which she recovered, in 1931 suffered from acute cholecystitis; gallbladder with over 1,000 small calculi removed. In 1934 streptococcal abscess of right lung Fæces examined October, 1934, numerous active *E histolytica.* Routine combined treatment—E B.I. and quinoxyl for 10 days—well tolerated Free from infection since.

(3) *Duration thirty-one years*

D B.B., 56, lived 21 years in India and 2 in Mesopotamia In 1910 amœbic dysentery with liver abscess (aspirated—two operations). Seven years later recurrence of amœbic dysentery treated by emetine injections, after which periodic attacks of diarrhœa Last 22 years in England. In June, 1941, sudden acute attack of diarrhœa with tenesmus, carcinoma suspected on account of wasting and cachexia Sigmoidoscopy revealed amœbic ulcers and fæces contained *E histolytica* cysts Combined E B I and quinoxyl treatment resulted in cure Put on weight, normal stools since.

(4) *Amœbic dysentery in boy of 15, duration 10 years, possibly longer*

A P.B, 15½, born in India, lived there till 5½ At seven months had first attack of dysentery (? amœbic) At 5 relapse, treated by emetine injections. Intermittent attacks of diarrhœa subsequently for 6 years. [illegible]

(5) *Duration 28 years, appendicostomy*

W C, 61, first attack of dysentery in S African war in 1901 Seen in February, 1929. During 28 years suffered intermittently with diarrhœa, blood and mucus In 1929, on supposition that he was suffering from ulcerative colitis, appendicostomy For 10 years continuously he irrigated himself daily through the wound In fæces cystic and precystic forms of *E histolytica* Combined E B I and quinoxyl enemata for 10 days Appendicostomy closed Reported June, 1941, in good health, no return of symptoms.

(6) *Duration 24 years.*

[illegible]

obtained. Ravaut's paste is usually given for a course of twelve days. It has been used a good deal in France

Drugs used for special symptoms. *Secondary diarrhœa*.—This diarrhœa occurs sometimes in a bowel which has been greatly damaged by amœbic ulceration, and various enemata have been advocated.—

(1) ℞	Quinin dihydrochlor. . . .	10 gr (0 65 grm)
	Acid. boric.	2 drachms (7.75 grm)
	Aq ad	2 pints (1,336 c c)

To be given at body temperature.

(2) ℞	Acid tann.	150 gr. (10 grm)
	Quinin hydrochlor . . .	15 gr. (1 grm.)

To be dissolved in 1¾ pints (1 litre) of warm water. (If pain is caused, use at half-strength)

Post-dysenteric colitis.—A kind of mucous colitis is frequently seen after amœbic infection This must be treated on the principles laid down for the treatment of that disease in Chapter XXIII

Post-dysenteric constipation.—Obstinate constipation may often set in. *The usual oily preparations such as liquid paraffin, petrolagar,* isogel or agarol may be employed; castor oil may be necessary, and salts also may be beneficial. The following mixture is recommended.

℞	Ferr. sulph . .	3 gr.
	Liq arsen . .	3 minims
	Inf aloei . . .	1 oz.

One ounce three times a day.

Proof of radical cure.—It is by no means easy to prove that a [illegible] curative *treatment,* whether active [illegible]

Illustrative Cases

(1) *Duration sixteen years.*

P.H C , 70, twenty years in India First attack of amœbic dysentery 1929, *treated by emetine injections* , *second attack* in England seven years later. Third attack 1939 , owing to loss of weight, diarrhœa, blood and mucus stools, suspected of carcinoma Sigmoidoscopy suggested amœbic ulceration, confirmed by scrape preparations Fæces contained large numbers of *E histolytica* cysts Combined E.B I and quinoxyl retention enema treatment for 10 days. Since then

THE SURGICAL ASPECTS OF AMŒBIC DYSENTERY

[illegible] other than liver [illegible]

[illegible] rectum or the cæcum, tuberculous enteritis, intestinal obstruction, [illegible] by acute hepatitis

Perforation of the cæcum may take place suddenly, or the process may be insidious, accompanied by formation of a localized abscess. Perforation of any portion of the colon may also occur, causing general peritonitis, localized pericolitis, or pericolic abscess Perinephric [illegible] and periproctitis with rectal stricture and fistulæ may occur * [illegible] fistulæ may result [illegible] the symptoms may not be so dramatic, and perforation may only be suspected when there is spreading abdominal tenderness and distension. If retroperitoneal perforation occurs, or if adhesions have formed round the attenuated area of the bowel-wall, abscesses may gradually form. Usually this gives rise to local pain and tenderness, most commonly in the right iliac fossa where it may closely resemble appendix abscess

The treatment of amœbic perforation is a surgical procedure, although usually these cases are recognized too late C C Choyce recorded two cases of successful suture of dysenteric ulcerations during the 1914-18 War (Private communication) In one there was a localized abscess shut off by adhesions, which was opened and drained : in the other a

* Z Cope (1920) records operating upon 12 cases of perinephric abscess of which four had a history of previous dysentery and two had amœbic cysts in the fæces He also records cases of periproctitis in which amœbæ have been demonstrated in the resulting fistulæ

liver enlarged, infiltration of sigmoid and large intestine. Combined E.B.I. and quinoxyl retention enemata. Reported regularly since in good health.

(7) *Duration 11 years, appendicostomy.*

L. P., 34, contracted amœbic dysentery in Burma in 1921. Emetine injections. Returned to England 1923. Case is remarkable on account of resistance to emetine and E.B.I. Had three separate courses of E.B.I. (30 grs.) in hospital. Acute relapses on each occasion within ... Regarded as incurable; ... ipecacuanha solution for ... *E. histolytica* in discharge ... ned E.B.I. (grs. xx) and quinoxyl enemata, also quinoxyl irrigations through appendicostomy. After 5 months appendicostomy wound closed, no dysentery since. Subsequently had ureteric calculus, passed *per urethram.*

Diet.—The problem of diet in the convalescent treatment of amœbic dysentery is rather a controversial subject. In the author's opinion, when efficient cure of intestinal amœbiasis has been attained the need for strict dietary does not arise, but for the present it is safer to adhere to a judicious dietary for at least one month from the cessation of ...

active treatment.

Permitted. Porridge, eggs, fish (haddock, plaice, cod, sole, or whiting, ...

tripe, brains, and sweetbreads are also permitted. Beverages—light wine or claret.

Not permitted. Cheese, new bread, potatoes, fats, suet puddings, rich cakes, pastry of all kinds, coarse fruit and vegetables (turnips or carrots, cabbage), pickles, sardines and preserved fish. Beverages—spirits, beer or stout.

...

costomy, as in bacillary dysentery, with the object of washing ... bowel. Indeed, recent experience goes to show that such should never be adopted, except as a last resort.

THE SURGICAL ASPECTS OF AMŒBIC DYSENTERY

Although the surgical complications of amœbiasis—other than liver abscess—play a considerable part in tropical practice, yet this important aspect has received scant attention in textbooks It has already been pointed out that amœbic dysentery may simulate many other diseases Symptoms may resemble those of hæmorrhoids, carcinoma of the rectum or the cæcum, tuberculous enteritis, intestinal obstruction, [illegible] by acute hepatitis.

Perforation of the cæcum may take place suddenly, or the process may be insidious, accompanied by formation of a localized abscess Perforation of any portion of the colon may also occur, causing general peritonitis, localized pericolitis, or pericolic abscess Perinephric [illegible] and autopsies in Java, has found that an extension of the inflammation through the bowel-wall often occurs, and gives rise to peritonitis with adhesions, sometimes also perirectal abscesses and recto-vaginal fistulæ may result

[illegible] round the attenuated area of the bowel-wall, abscesses may gradually form Usually this gives rise to local pain and tenderness, most commonly in the right iliac fossa where it may closely resemble appendix abscess

The treatment of amœbic perforation is a surgical procedure, although usually these cases are recognized too late. C C Choyce recorded two cases of successful suture of dysenteric ulcerations during the 1914-18 War (Private communication) In one there was a localized abscess shut off by adhesions, which was opened and drained in the other a

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leak was found in the terminal portion of the ileum, which was sutured, and with free drainage the patient recovered. If the perforation cannot easily be closed, the affected loop should be drained extraperitoneally.

emphasized that, in every country where amœbic dysentery is endemic, the surgeon should have the fæces examined for amœbæ or cysts before deciding upon operation.

malaria a condition may arise which closely simulates it. Z. Cope advocated the thigh-rotation test as useful in determining whether tenderness per rectum is due to ulceration of the pelvic colon or to a perforated appendix

Thrombosis of the portal vein as a surgical complication of intestinal amœbiasis has been described by A. E. Sitsen (1913).

Fulminating amœbic dysentery.—The dysenteric process is sometimes so acute that large portions of mucous membrane become gangrenous and slough, with spread of infection through the bowel-wall into the peritoneal cavity. In this condition the surgeon may be asked to operate, either to provide an opening for washing out the colon from above, or to divert the intestinal contents and thus give the colon a rest. For the former purpose appendicostomy or cæcostomy is the operation of selection: for the latter, ileostomy.

As a general rule, surgical interference in intestinal amœbiasis is strongly contra-indicated Whenever it has been somewhat recklessly undertaken, disaster has resulted This was the experience during the Chicago epidemic of *1933–34* *In the author's experience*, when a colostomy has been undertaken in amœbiasis on the mistaken conception that the symptoms are those of carcinoma, amœbic ulceration is accentuated rather than retarded. In September, 1937, the author had such a case under his care—an ex-soldier from India, twenty-five years of age (*see* p 250) Colostomy had been performed to relieve

application of styptics. Subsequent to any operative measures the

granuloma may necessitate a short-circuit operation

Immunity.—Although there is nothing definite known about immunity to infections with *E. histolytica*, such evidence as we possess

This has been found to be the case, certainly, in experiments on animals. Immunity to infection with *E. histolytica* is probably dependent primarily upon the resisting power of the host. These are the clinically observed facts, while a considerable amount of tentative work on immunity reactions of amœbiasis has been carried out in laboratory animals (*see* p. 154).

Prophylaxis.—The measures adopted to prevent infection with *E. histolytica* are practically the same as those already described for bacillary dysentery, and depend in the first place upon efficient sanitation and measures directed against the house-fly, which may act as a carrier of amœbic cysts. It must be especially insisted that, in the tropics, raw vegetables, lettuce, fruits, and foods which have been exposed to the air and possibly contaminated by human excreta, must be avoided. The prevalence of intestinal amœbiasis in heavily cultivated districts is undoubtedly due to the prevailing custom of fertilizing with human night-soil. The cysts of *E. histolytica* can survive in a moist medium, and there is considerable evidence that the disease is in the main water-borne; thus, in large communities, the problem resolves itself into the provision of a pure water supply.

The question of dealing with human carriers of *E. histolytica* cysts is difficult. It is probably advisable that, in the tropics, where a large number of native servants are employed, fæces should be examined periodically for cysts of *E. histolytica*, and no cyst carrier should be employed as cook, waiter, or mess orderly. Wherever possible, infected individuals should be treated with emetine-bismuth-iodide, and the source of infection removed.

As C. F. Craig (1935) rightly points out, amœbiasis must be regarded as a public health problem in those countries where it is endemic, as it has been proved to be in parts of the United States. The evidence shows that it is present in parts of that country, and that 5–10 per cent. of the population harbour *E. histolytica*.

Successful prevention and final eradication of amœbiasis depend upon general sanitation, pure water supply, and protection of food from flies Efficient sterilization of drinking water is most necessary. This cannot be effected by chlorination but is more efficiently done by filtration (B. K Spector, J. R. Baylis, and O. Gullans, 1934). The former method does not destroy the cysts of *E. histolytica*

CHAPTER XIV

AMŒBIASIS (*continued*): SECONDARY AMŒBIASIS*

In secondary amœbiasis the liver is the organ most frequently affected, resulting, as a rule, in amœbic hepatitis or in hepatic abscess

Amœbic hepatitis or hepatic amœbiasis.—Acute amœbic hepatitis may supervene at any time during the course of amœbic infection in about 5 per cent of cases. It may come on while symptoms are acute, or it may appear as a " bolt from the blue " during a remission of the disease It may be accompanied by alarming symptoms and is usually preceded by a rigor The patient complains of dyspepsia, acute

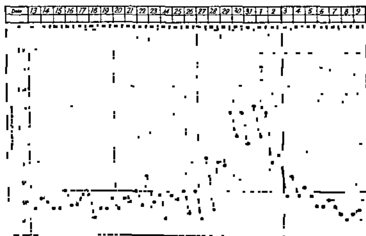


Chart 3—Amœbic hepatitis occurring during chronic amœbic dysentery. Note immediate response to emetine therapy.

precordial pain, and a heavy sensation over the hepatic area Sometimes, when the onset is not quite so acute, he may become conscious of a sharp stabbing pain over the liver, accentuated by any jarring movement The temperature may rise to 103° or 104° F The face is flushed, the tongue furred, and the patient obviously in great pain The liver itself is usually greatly enlarged—the lower border may

*The historical aspects of this subject have been ably set forth by W A E Karunaratne (1940-1)

project for more than a hand's breadth below the costal margin—and extremely tender Pain referred to the right shoulder area is also frequently present Onset of hepatitis is accompanied, as a rule, by exacerbation of the dysenteric symptoms and diarrhœa. The pulse is rapid and dicrotic and profuse diaphoresis is common. A distinctive feature is a considerable leucocytosis 20,000–30,000.

Acute hepatitis may subside in three or four days without active treatment. The condition yields to emetine therapy (Chart 3), and the liver diminishes rapidly after incision and operation, or after [illegible]

A nice point in differential diagnosis is the distinction between acute amœbic hepatitis and acute cholecystitis—by no means always easy. In cases of doubt, assistance may be sought in the marked leucocytosis which is associated with hepatic amœbiasis, its connexion with previous [illegible]

when there are signs of obstructive icterus, then amœbiasis can be ruled out, but toxic jaundice may occasionally accompany hepatic amœbiasis.

[illegible]

circumstances [illegible] liver [illegible] be [illegible] bly, [illegible] the [illegible] the [illegible]

injection of emetine.

Occasionally *relapsing cases* of acute amœbic hepatitis with multiple rigors may occur. The following is an illustrative case :—

became apparent as the disease progressed The leucocytes numbered

by the appearance of intramuscular abscesses due to quinine injections given by his former medical attendants under the mistaken impression that the rigors were of malarial origin

Hepatic abscess (Liver abscess; Amœbic abscess of liver) — There can now be no question of the existence of an intimate relationship between intestinal amœbiasis and liver abscess, as numerous and well-authenticated statistics go to prove Hepatic abscess is, however, not always associated with obvious clinical dysentery; therefore the absence of a positive history of amœbic infection, or of diarrhœa, does not rule out the possibility of an amœbic liver abscess

The association of intestinal symptoms with liver abscess has long been recognized, but it cannot be said that, until comparatively recently, information on the subject was either well-defined or precise Since 1887 it has been generally accepted that tropical liver abscess is, in fact, but a complication of intestinal amœbiasis The actual invasion of the capillaries of the bowel wall by amœbæ and their subsequent transportation to the liver was first observed by H F Harris (1898) It is especially likely to attack Europeans, in contra-distinction to natives of those countries in which amœbiasis is endemic In the Indian Army in 1894 the proportion of deaths from liver abscess to the total mortality was estimated, in native troops, at 0 6 per cent, whereas in European troops it was 7 4 per cent It is unquestionably true that amœbic abscess of the liver was much more frequently encountered in

Undue consumption of alcohol was formerly considered a potent predisposing cause thus in forty cases of liver abscess, E J Waring noted intemperance in 67 5 per cent Few authorities at the present

cæcum or in the ascending colon (sixty-three cases, with dysentery findings in 90 5 per cent) Liver abscesses have been found frequently in association with fatal amœbic dysentery (C F Craig (1931) 83 per

cent.; A. E. Sitsen (1927) 10 per cent.; A. C. Clark (1925) 51 per cent.) Chauffard (1892) has epitomised as follows:—"The more

Ætiology.—Liver abscess is apparently likely to occur in about 2-5 per cent. of amœbic infections in Europeans, but to a much smaller degree in natives of the endemic zones.*

As a general rule, liver abscess occurs in those Europeans who have long been resident in the country; it is not a disease of the newcomer.

It is well known that European women in the tropics, though as

however, in Cairo, reported an amœbic liver abscess in a child of three months.

P. Huard and J. Meyer-May (1936) record a series of 150

in 745 cases, slightly over 5 per cent.

PATHOLOGY OF HEPATIC AMŒBIASIS

Probably the liver becomes invaded by *E. histolytica* via the portal vein. It has already been stated that, in sections of the bowel, amœbæ

vessels

quency

of pleurisy in hepatic abscess; according to this view pleurisies may be divided into those which are the result of direct extension and those which are of metastatic origin. Councilman and Lafleur (1891) originally demonstrated amœbæ in the exudate on the surface of

* Probably the estimates which placed the incidence of amœbic abscess at 20 per cent., e.g., in Councilman and Lafleur's series in 1891, were exaggerated. A. Davidson, writing in 1907, states that 8.5 per cent. of those suffering from amœbic dysentery developed liver abscess.

the liver, but there is no evidence that they can enter by the peritoneal surface or by the bile ducts. Ch. Dopter and K. Deschiens (1938) have, in fact, shown that the presence of bile salts in culture media retards the development of *E histolytica* The capacity possessed by the liver for regeneration is remarkable. The liver outside the abscess area may have a normal appearance, or may show varying degrees of congestion.

The liver of an infected person is subject to constant attack by invading amœbæ If, however, they are unable to obtain a footing, they soon perish, as the hepatic cells appear to be able to arrest further multiplication of *E histolytica* Unless they are able to produce large areas of necrosis, hepatic abscess does not ensue

The production of numerous small necrotic areas a few millimetres in size, containing gummy pus, with actively dividing forms of *E. histolytica*, results in amœbic hepatitis, (Fig 25) and may not necessarily precede a genuine hepatic abscess

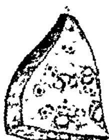


Fig. 25.—Miliary necrotic foci in liver in acute hepatic amœbiasis, with portal distribution of the entamœbæ

G B Bartlett (1917) found hæmorrhages in the central zones of the liver lobules, and insular cirrhosis has been noted by other observers, both this and necrosis are the results of metabolic and chemical toxins In sections through the wall of an acutely-spreading abscess the amœbæ may readily be seen in the blood-vessels This appears to be the result of a much more gradual and insidious process, though the factors which govern the behaviour of amœbæ in the liver and the subsequent pathological effects brought about by their presence are not entirely understood When once amœbæ have become established, they multiply as they do in the intestinal wall, causing coagulation-necrosis, and formation of abscess cavities Several primary centres then coalesce, the cavity becomes occupied by what is usually termed "liver-abscess pus," which is really gummatous matter consisting of dead liver cells in all stages of disintegration, but where this process is not so complete, washleather-like sloughs are formed Liver abscess pus is the result of breakdown of the liver cells and not of suppuration, and appears as a reddish-brown or chocolate coloured substance, resembling anchovy sauce, usually sterile in the bacteriological sense

two In H J Waring's series (1897) abscesses were single in 61.5 per cent, double in 11.5 per cent.; and multiple in 27 per cent In 189 cases, Huard and Meyer-May (1936) found that in 102 cases the abscess was situated in the anterior portion of the right lobe, and in 87 in the posterior portion They found a proportion of 137 cases of single to 13 of multiple abscess

E Sambuc of Cochin China, in a classification of eighty-seven cases of liver abscess (1918), found that in :—

56 cases	there	was	1	abscess
11	,,	,,	were	2	abscesses
10	,,	,,	,,	3	,,
2	,,	,,	,,	4	,,
1 case	,,	,,	,,	5	,,
1	,,	,,	,,	8	,,

According to L Rogers (1913), in India, in 70 per cent. of cases the abscess is single Among thirty-eight cases of more than one abscess, two were found in 44.7 per cent., three in 20.3 per cent,, four in 18 4 per cent, and over four in 10 6 per cent.

The left lobe is rarely infected, the Spigelian lobe even more rarely. In ninety-five cases of amœbic abscess observed at autopsy, [illegible]

[illegible] lobus Spigelii. Out of 6[illegible] cases collected by Rouis (18[illegible]) [illegible] per cent were in the right lobe, 13 3 per cent in the left In 756 autopsies (F[illegible]) [illegible] inferior, 47

	Right lobe Per cent	Left lobe Per cent.
Huard and Meyer-May	92	8
Fontan	97	3
Chatterji	78	22
Sir L. Rogers	88	12

L. R Cleveland and E. R Sanders (1930) appear to have proved, in their experimental work on cats, that in these animals amœbæ introduced into the liver fail to set up pus-formation, unless bacteria are also present These workers favour the idea that some symbiosis exists between the protozoan and bacteria.

A typical liver abscess increases in size until it may involve nearly the whole organ (A. I Ludlow, 1926), and the largest may attain the size of an average coco-nut. A whole lobe, or even the entire organ, *may be converted into a bag of pus, the capsule forming the sole wall* Waring has recorded two cases in which a gallon of pus was found As it enlarges, so the cavity continues to fill with cytolysed liver cells, necrotic tissue, and blood, the process advancing so rapidly that *no pyogenic membrane is formed* At this stage the pus may sometimes become secondarily infected with micro-organisms such as *Bacillus*



Fig. 26.—Formation of liver abscess Complete microscopic section of right lobe of liver, showing two amœbic abscesses. Numerous *E histolytica* are visible microscopically within the marked circle.
(½ *nat size*)

coli, *B enteritidis* (*see* p 223) or streptococcus, and in these cases its character changes and it becomes green At any time a liver abscess may become arrested and encapsulated The pus is then partially absorbed and resembles thick cream cheese, ultimately, it may become calcified, the walls under these circumstances are often smooth and fibrous On the other hand, complete absorption may take place, and A. S. Fry (1924) mentions two cases of large hepatic abscesses in which the cavities were obliterated, leaving a cicatrix

In long-standing abscess pus, the causative amœbæ eventually die out altogether. Amœbæ are usually difficult to find when the abscess is first opened, but when the cavity has been exposed to the air, they

appear. It was suggested by W. E. MacCallum (1937) that their need

i amœbic abscess may cause a

it lies deeply, and can be seen only on incision; this is specially noticeable when multiple abscesse are present. The liver is generally enlarged, and fatty degeneration and venous congestion may be present, but wherever the abscess is in contact with the peritoneum, there is a localized peritonitis and adhesion of the liver to the dome of the diaphragm. According to Z. Cope (1920), the marked enlargement occasionally seen with a comparatively small abscess is due to great exudation of serous fluid. Thrombosis of radicles of the portal vein may ensue.

Old abscess cavities are enclosed in a wall of connective tissue; internally the abscess wall is covered with necrotic tissue causing a peculiar shaggy appearance.

Histopathology.—In the early stages, the necrotic débris constitutes an area of cytolysed tissue cells, in which red blood-corpuscles, degenerated liver cells, a few leucocytes and connective-tissue cells may be seen. In older abscesses, the ill-defined wall consists of connective tissue, and the cavity is filled with necrotic liver cells and cytolysed

uncommon

L. Hirtzmann (1922) has described engorgement of the capillary vessels with chains of amœbæ and surrounding aggregations of eosinophil cells.

The Bilaterality of the Liver

Until quite recently it has never been stated in any textbook that there is

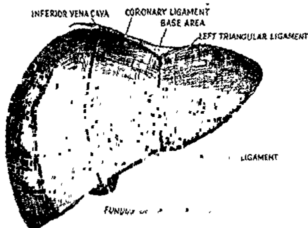


Fig. 27.—Superior surface of liver to show surface markings of the plane division.

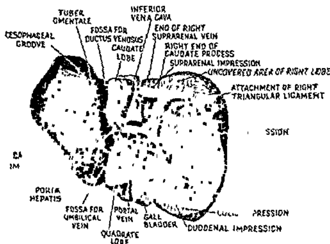


Fig. 28.—Inferior surface of the liver, showing the line bounding the plane of separation of the right and left lobes.

the back of the liver; this, then, may be termed the mid-line of the liver.
... and also by the investiga-
... ed the portal vein,
... e thus able to show
... larly and definitely
... urther that, except
... cient to maintain a
... s the line of separa-
... c artery are separ-
... e line of separation
... that of the artery
... 7, 28.) W. Sérégé
... splenic vein of the
... lobe only, whilst in

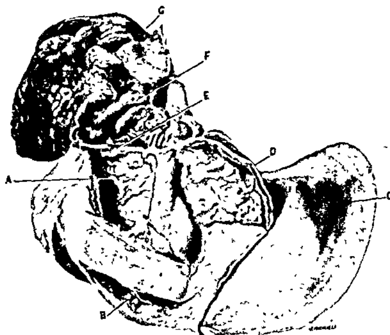


Fig. 29.—Amœbic liver abscess, showing hypertrophy of left lobe.

Th... abscess containing a pint of pus
... There

represent the true embryological right and left hepatic lobes, and that the falciform ligament, hitherto adopted as a division between the right and left lobes of the liver, is merely an arbitrary landmark

The experience of recent years has verified the premises The author's case, shown in Fig 29, is another instance of the destruction of the right lobe [illegible]

[illegible]

secondaries are spread by the lymphatics, which do not divide as do the portal vein and bile-ducts

SYMPTOMATOLOGY OF HEPATIC ABSCESS

[illegible]

abscesses which had destroyed the greater part of the liver without producing the generally recognized clinical picture

As a rule, the patient is one who has long resided in the tropics and may at some time or other have suffered from amœbic diarrhœa or subacute attacks of dysentery. He becomes conscious, at first, of an uneasy sensation over the liver and in the right hypochondrium, and later begins to suffer from sharp stabbing pain in the hepatic area, accompanied by a dry cough In a certain number there is also a sensation of rheumatic-like pain radiating around the right shoulder-joint, especially during the night It may extend downwards as far as the angle of the scapula, and the skin over the acromial area is tender to the touch This pain is now recognized as reflex and due to irritation of the phrenic nerve by stretching of the diaphragm, transmitted through the third and fourth and sometimes the fifth cervical nerves, to the supra-acromial and supra-clavicular cutaneous branches So characteristic is this pain that, in abscesses of the left lobe of the liver, it may be referred to the left shoulder-joint In 300 fatal cases described by E J Waring (1854), pain in the shoulder region was recorded in forty-eight

Soon, other symptoms become apparent; the patient becomes feverish, particularly towards night-time, and may experience a few short rigors Accentuated rigors such as have been described in amœbic hepatitis, are, however, rarely seen The tongue becomes furred, the appetite is lost and the patient soon begins to lose weight His complexion assumes a curious yellow subicteric tinge, in fact, what

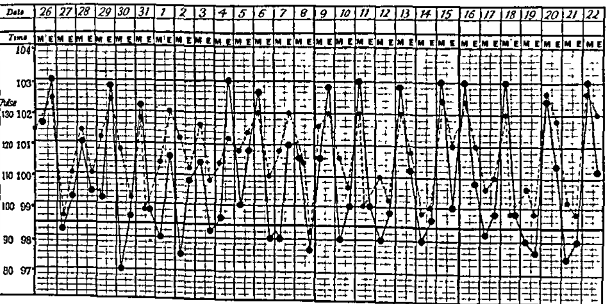


Chart 4.—Fatal case of amœbic abscess of liver, showing tertian type of pyrexia. The dotted line indicates the pulse-rate.

is generally described as "a muddy look." The quotidian rise of temperature now becomes a regular feature of the illness, and the thermometer towards 10 p m may reach 102° F, even 104° F., sinking to normal or subnormal during the morning. These pyrexial bouts are accompanied by profuse sweats, which necessitate a frequent change of clothing during the night Insomnia, or restlessness at night, is usual Occasionally a tertian type of temperature is encountered (Chart 4)

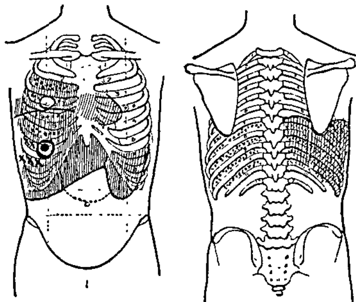


Fig. 30.—Liver abscess with rupture through the diaphragm, secondary pulmonary abscess, and compensatory hypertrophy of left lobe of liver.

Dilated stomach, considerable secondary anæmia and *E histolytica* cysts in fæces. Note physical signs at base of both lungs. Death from streptococcal septicæmia. Indian infection of 11 years' latency ⊙, site of abscess, XXX, pleuritic rub

During the daytime the patient's extremities are cold and clammy

found over the right rectus muscle in the gall-bladder area, which is deceptive as it may lead to a diagnosis of cholecystitis

[illegible]

of this note, which differs in tone from that of chronic venous congestion or other conditions. Deep inspiration may give rise to acute pain, and sometimes one or two especially tender spots may be discovered in the lower intercostal spaces Unless the disease is complicated by malaria, the spleen is not enlarged; but, as pointed out on p. 210, a tumour in the left hypochondrium, which is separated by a resonant zone from the left lateral margin, may be due either to an independent abscess of the left lobe of the liver, or to compensatory hypertrophy (Fig. 30)

On auscultation a pleuritic rub may be detected at the base of the right lung and over the whole of the hepatic area, or there may be *extensive signs of compression of the base of the right lung.* Sometimes

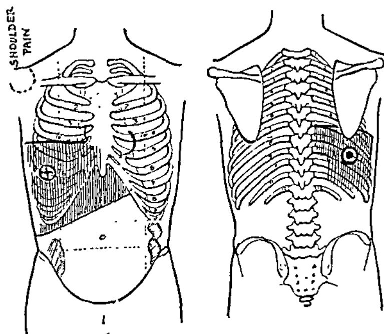


Fig. 31.—Liver abscess, Indian infection with shoulder pain, no E. histolytica cysts in fæces; leucocytes, 22,000.

Three preliminary aspirations. No reaction to emetine Open operation ⊕, point of maximum tenderness, ⊙, site of abscess.

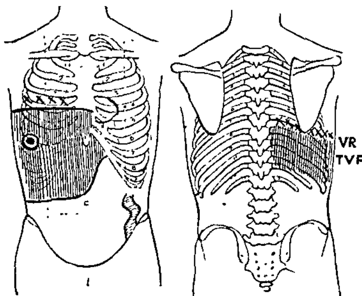


Fig 32.—Liver abscess, Indian infection, with *E histolytica* cysts in fæces; leucocytes, 18,000

Preliminary aspiration, 30 fl oz, subsequently open operation, Carrel Dakin drainage XXX, friction rub, VR, vocal resonance diminished, TVF, tactile vocal fremitus diminished; ⊙, site of abscess.

an effusion of fluid into the pleura may be present, which is, as a general rule, serous in character. It may be abundant, and on aspiration may prove to be genuine liver-abscess pus, and may contain active *E histolytica* It will thus be realized that to the tropical physician,

In less extensive cases, a decrease in the breath-sounds, a few inspiratory crepitations, or a diminution of the vocal fremitus may be noted. Pain is usually relieved by lying upon the affected side

As the case progresses, so the patient becomes more and more emaciated, and the fever with nocturnal sweats increases On the whole, general enlargement of the liver becomes more obvious, and percussion

found over the right rectus muscle in the gall-bladder area, which is deceptive as it may lead to a diagnosis of cholecystitis

Less frequently the liver dullness extends an inch or more above normal level in the nipple line and, on percussion, it can be observed that the line of dullness is altered by changes in position, when the patient lies on his left side, or stands up Attention must be drawn to the flatness of this note, which differs in tone from that of chronic venous congestion or other conditions Deep inspiration may give rise to acute pain, and sometimes one or two especially tender spots may be discovered in the lower intercostal spaces Unless the disease is complicated by malaria, the spleen is not enlarged; but, as pointed out on p 210, a tumour in the left hypochondrium, which is separated by a resonant zone from the left lateral margin, may be due either to an independent abscess of the left lobe of the liver, or to compensatory hypertrophy. (Fig. 30)

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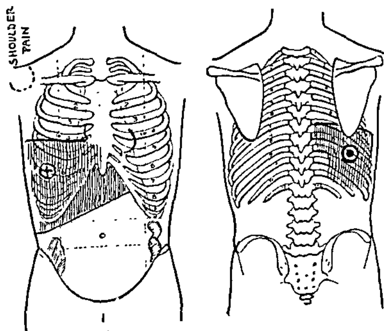


Fig. 31.—Liver abscess, Indian infection with shoulder pain, nò *E histolytica* cysts in fæces; leucocytes, 22,000.

Three preliminary aspirations. No reaction to emetine Open operation ⊕, point of maximum tenderness, ⊙, site of abscess.

Enlarged cervical and axillary glands may sometimes be observed on the affected side, while the rheumatic-like pain and swellings, which are apt to accompany any chronic infection may cause difficulties in diagnosis

pressure and show tachycardia and irregularities

Swellings of the epigastrium or hypogastrium, closely simulating

In order to appreciate the frequency of particular symptoms in hepatic abscess, the following tables have been constructed from a series of the author's cases over a period of ten years —

TABLE XII

Total Number of Liver Abscess Cases, 45

Ages, 16–63
Sex males, 39, females, 6
Deaths, 3 (6 per cent), one from toxæmia, one from septicæmia, one from pneumothorax

cent.)

Pyrexia —

In upward direction, 11 (24 per cent)

may now disclose a tender area or local œdema of the chest wall, which indicates the direction at which the abscess is pointing. Unless relieved by operation, the patient dies worn out by emaciation after months of prolonged misery; or the abscess, which by now may have

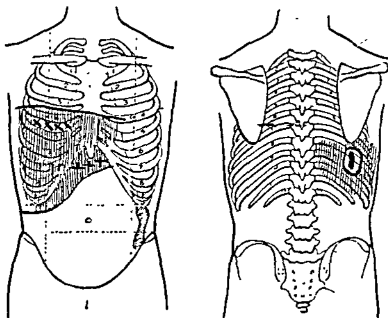


Fig. 33.—Liver abscess, Iraq infection, with active *E. histolytica* in fæces; leucocytes, 23,000, and pleural effusion at base of right lung. Latent period, 12 years.
Open operation + Carrel-Dakin irrigation, + E B I. medication. XXX, friction rub; ⊙, site of abscess.

Although the foregoing account can be taken as describing the average

distinctly quotidian or intermittent.

developed

A second instance occurred in a girl of sixteen who was seen in 1928 She

years of age

occurred in 75 per cent of the series, in only 24 per cent was it enlarged upwards towards the nipple line

Although there is usually considerable enlargement of the liver, yet there may be none. In the author's series a large abscess has been found to contain two pints of pus or more in a case in which an X-ray film and screening of the diaphragm had shown nothing abnormal

Jaundice is infrequent in an uncomplicated liver abscess but may occur through pressure on the hepatic ducts, according to Z. Cope. Bile in the discharge from a liver abscess sinus may be due to rupture into the common bile duct

Rupture —An amœbic abscess may rupture into almost any contiguous organ, and thereby a spontaneous cure may be produced (Fig 94) Usually it bursts into lung or pleura. When it ruptures into the lung, the contents are suddenly coughed up as dark pus mixed with blood, so that the patient may be almost suffocated On the other hand, rupture may not occur so suddenly, in this case the

Many years ago Manson pointed out that rupture through the diaphragm resulted in a valve-like aperture, so that the abscess

Obvious swelling of chest wall, 3 (6 per cent.).

2 per cent.; large mononuclears, 6 per cent.; eosinophils, 1 per cent.

Grave anæmia, 8 (17 per cent.) Most severe anæmia noted · R.B.C. 1,375,000, hæmoglobin, 40 per cent (*See* p. 232)

There are no records of liver abscess in a person who has been resident in the tropics under
varies from two to three y
history of diarrhœa or dys
of the cases, while cysts of
in only two cases were entamœbæ present in the fæces, together with active dysenteric symptoms

It is a curious observation to which J Twining, as long ago as 1852, drew attention, that, so soon as a liver abscess becomes established, any dysenteric intestinal symptoms which were previously apparent, subside

In this series, too, the abscesses were solitary, except in one very rapidly fatal case, in which they were multiple. In the majority of the forty-five cases the abscess was situated in the upper and posterior part of the right lobe of the liver, and in five it was situated in the left lobe.

Usually the accompanying fever was of a hectic, frankly remittent character, with nocturnal excursions, in two cases the fever was so

abscess, often
usually in these
the diagnosis
This has also
1933 in Cairo

An ex-officer was seen in 1921 after service in East Africa On account of his extreme emaciation and anæmia, and also on account of the chronic

There may be nothing in the patient's appearance to suggest a liver abscess, for the facies may show no sign of the condition, which may

may, however, become secondarily infected with amœbæ, with resulting ulceration.

Chronic suppuration from a liver abscess may lead to amyloid disease, a rare complication which is seldom encountered in modern practice, as in the case recorded below :—

The patient had spent most of his life in the Transvaal, and his illness was of some seven years' standing It began with what was considered to be a right sided pleurisy, which necessitated rib-resection and residence of five months in hospital In 1930, amœbic dysentery declared itself and a liver abscess was suspected, two years later a large collection of pus was noted in the left pleura, and eventually thoracoplasty had to be performed, the pus which was evacuated was of "anchovy-sauce" character For the first time emetine was exhibited, with excellent results.

waxen, yellow facies of amyloid disease, and a grave prognosis was given

Mortality.—In the early years of last century the case mortality from liver abscess was very high—something like 50–80 per cent—specially in the British Army Owing to advances in diagnosis and treatment, however, the death rate has since fallen very considerably, so that deaths from liver abscess are extremely rare at the present day When death ensues it may be due to pressure of the abscess itself, to secondary infection by streptococci or *Bacillus coli*, to gangrene of the abscess wall, to pneumothorax, to anæmia, or to some intercurrent disease In the author's series of forty-five cases there were three deaths, one being due to pneumothorax, and two to septic infection of the abscess cavity The mortality rate was 6 per cent, and this probably represents the average death rate at the present day

Diagnosis

There are few serious tropical diseases so frequently overlooked as liver abscess, this is due to the variety of symptoms As a French surgeon has put it, "it is easier to operate upon a liver abscess than to diagnose it" The diagnosis is more easily arrived at in the acute than in the chronic cases.

The following are mistakes commonly made in diagnosis :—

(1) Failure to recognize the presence of any disease,

(2) Misinterpretation of the signs at the base of the right lung

febrile process;

(4) Mistaking other diseases, such as non-suppurative hepatitis or the hepatitis found in association with malaria, etc for abscess of the liver.

abscess becomes chronic, and is accompanied by other signs of pulmonary absorption, such as respiratory distress and clubbed fingers. Sudden rupture may result in the swallowing of much blood, and consequent melæna

Rupture into the pleura is by no means as common as rupture into *the lung. It may lead to a suddenly developed pleural effusion and* the signs of empyema, and in one particular instance the author was able to demonstrate amœbæ A distinctive character of the cellular

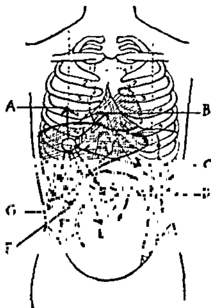


Fig. 34.—Diagram to show possible directions in which a liver abscess may burst.

A, lung, B, pericardium, C, stomach, D, duodenum; E, peritoneal cavity, F, cæcum, G, perirenal fat.

picture may be the high proportion of eosinophil cells, as described by V. Cordier and L. Morenas (1930).

Finally the abscess may rupture through the [illegible] wall, and evacuate itself painlessly; this is the most fortunate and natural termination The skin around such a spontaneous rupture

is the differential diagnosis from perinephric abscess and pyonephrosis The author has encountered two cases of perinephric abscess which had been mistaken for abscess of the liver, in one, drainage through the liver had actually been instituted, and the true nature of the disease remained unrecognized till revealed by radiography (Fig 85) An important point is the differential diagnosis from subphrenic abscess (*see* p 229) Carcinomata of the liver may simulate abscess so closely, and may give rise to such hepatic and pulmonary signs as almost to defy differential diagnosis, save by laparotomy

Liver abscess may occur in association with *Ascaris lumbricoides*, through migration of this parasite into the common bile-duct (Girges), it has been reported, too, in the glanders-like disease melioidosis (Stanton and Fletcher)

as with diverticulitis

Case illustrating peculiar difficulties in diagnosis.

In 1938 the patient had been invalided from India with a continued pyrexia

restricted movement of the right diaphragm and a circular less opaque area in the liver substance, but there was no leucocytosis, the count being 6,400 with

abscess

Cases illustrating points of differential diagnosis.

Differential diagnosis.—The differential diagnosis of liver abscess, considered *in extenso*, is a large subject, and presents many practical difficulties. Differentiation has to be made from all the other febrile conditions it may simulate: from the continued fevers, such as typhoid, undulant fever, and tuberculosis, and from intermittent fevers, such as malaria. Indeed, Manson remarked that he had never encountered a liver abscess in European practice which had not previously been saturated with quinine, and that it should be considered a golden

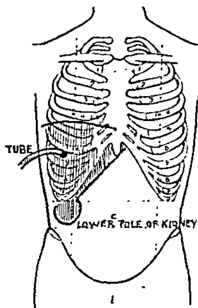


Fig. 35.—Perinephric abscess regarded as liver abscess. Diagnosed by cystoscopy and lipiodol injection and opened through diaphragm.

Calculus in right ureter, streptococci in urine, leucocytes, 19,000

rule to suspect hepatic abscess in all cases of abdominal disease associated with an evening rise of temperature.

[illegible]

and less persistent rigors, undulant fever rarely associated with rigors,

nvolving the
llous abscess
hydatid cyst
yema of the

suppurative cholangitis with numerous secondary pyæmic abscesses in the liver proved the correct diagnosis (Chart 6.)

From malignant disease of the liver.—A retired regular soldier, aged fifty six

September, 1930

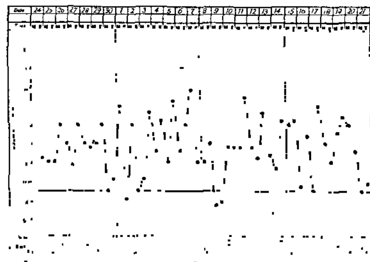


Chart 6.—Suppurative cholangitis due to gall-stones simulating amœbic abscess of liver.

was protuberant ; sclerotics and skin were slightly icteric ; and there were

tion disclosed doming and bulging of the diaphragm, as in liver abscess, with definite fixation

So far, the signs and symptoms pointed to abscess formation within the

February, 1925

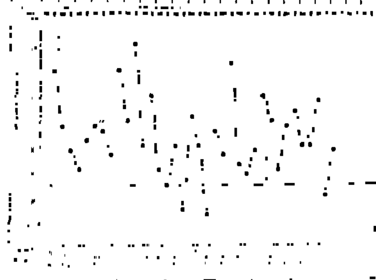


Chart 5.—Ascending pyelophlebitis secondary to an appendix abscess, simulating amœbic abscess of liver.

liver, but the presence of icterus could be taken as against the amœbic origin of the disease

The probability of extensive intra-abdominal suppuration received support

the response is almost immediate The character of the temperature chart, the frequent rigors, the persistence of urobilin in the urine, a

[illegible]

Paralysis of right dome of diaphragm.—A case presenting particular difficulties in diagnosis by reason of the X-ray appearances was seen in a Norwegian

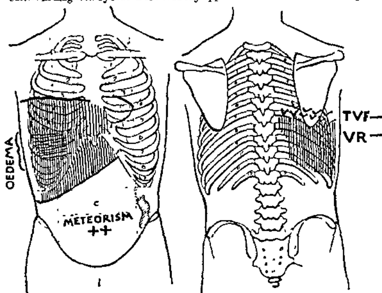


Fig. 36.—Carcinoma of liver primarily diagnosed as amœbic abscess.
Loss of 35 lb in weight, slight œdema of legs VVV, ægophony TVF, tactile vocal fremitus, diminished VR vocal resonance, diminished

[illegible] in 1941 There was great enlargement of the liver [illegible]

[illegible]

cirrhosis of the liver with collapse of the lower lobe of the right lung declared itself

From a suppurating gumma of the liver distinction may also have to be made This does not often arise—some three times in the author's experience Usually there are other stigmata of syphilis to be noted and the Wassermann reaction is positive

One disquieting feature was the appearance of a trace of bile and an excess of urobilin in the urine, but the Van den Bergh reaction was within normal limits.

Operation was advised, and disclosed a small primary carcinoma of the stomach, with numerous secondary nodules in the liver.

From cholecystitis, empyema of gall-bladder, gumma, and hydatid cyst.—The differential diagnosis from empyema of the gall-bladder, or even from cholecystitis, may give rise to difficulty, especially when the abscess is situated, as it so often is, in the anterior portion of the right lobe.

Amœbic abscess of liver (left lobe) simulating acute cholecystitis—*March, 1936*

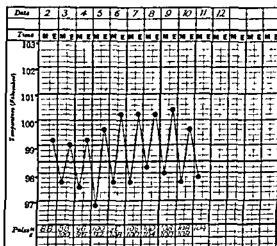


Chart 7.—Carcinoma of liver with pyrexia simulating amœbic abscess.

W F C , 35, examined in June, 1939, from Sudan. Previous history attacks of malaria at intervals, typhoid 1927, paratyphoid 1930. Recent recurrent attacks of fever (T. 102° F.) with severe subcostal pain. No history of dysentery
Leucocytosis 21,000 (
rectus muscle Pain on
gram showed dilated
diaphragm seen by X-

benign cystic adenomata These cysts are usually situated in the right lobe of the liver

Differential diagnosis from subphrenic abscess—Subphrenic abscess is less commonly seen at the present time than formerly The usual cause is perforation of a gastric or duodenal ulcer; out of seventy-six cases recorded by H. L Barnard (1910), it was due to perforation in twenty-six, the ulcer being gastric in twenty-one and duodenal in five The left anterior intraperitoneal fossa was usually affected This fossa is bounded above by the diaphragm, to the right by the left lobe of the liver, and to the left by the spleen, and by adhesions of the omentum to the abdominal wall (Fig 37)

mid-axillary line and may easily lead to a mistaken diagnosis of pneumothorax

When the perforation is at the pylorus, in the duodenum, or in the appendix, the right anterior intraperitoneal space may be affected Out of twenty seven abscesses of this type recorded by Barnard, four were the result of a perforated gastric ulcer, and two were from perforation of a duodenal ulcer The fossa in these cases is situated behind

gastric and one to a duodenal ulcer Rarely, the abscesses involve the lesser sac of the peritoneum (the left posterior intraperitoneal situation of Barnard) Two cases of this kind, out of three, were due to a perforated gastric ulcer, but the lesser sac was not affected alone

These are the physical characteristics of subphrenic abscess It will be seen that the maximal signs and symptoms are situated below the diaphragm and that there is absence of those signs which indicate actual destruction of liver substance As in liver abscess, however, unless the condition is relieved, the pus may find its exit spontaneously, the abscess bursting into a bronchus, into the pleura, with the formation of a pyopneumothorax, or into the stomach or intestine It rarely

A case of this description was seen by the author together with Mr. H. E. [illegible]

The associated symptoms are by no means so characteristic, and as aids to diagnosis the eosinophilia which accompanies hydatid infection

Fig. 37.—Abdominal signs in anterior (gastric or duodenal) variety of right *anterior intraperitoneal subphrenic abscess.*

F, falciform ligament bulging to left, A, band of adhesions from umbilicus to costal margin P, pus in contact with abdominal wall, G, gas-bubble over liver dullness, U, umbilicus, E, ensiform, C M, costal margin

and the intradermal Casoni test (which is valuable) must be taken into account

From non-parasitic cysts of the liver.—R. Maingot (1940) has described these as single or multiple, more common in females than males [illegible]

[illegible] associated with cysts of kidneys, pancreas or other organs or polycystic disease. Solitary non-parasitic cysts of the liver are congenital, of biliary origin, perhaps *arising from aberrant bile ducts, resulting* in

9,000–35,000 in 88 per cent of the author's series. It must be noted that, in contradistinction to pneumonia and other septic conditions, the total increase of the leucocytes is seldom very high The average is about 15,000 An actual increase of polymorphonuclears above 80 per cent *is rare; in the author's records this occurred only six* times The highest differential count recorded was 88 per cent and once there was a polymorphonuclear count as low as 35 per cent As a general rule, the leucocytosis is higher with acute accumulations of pus, and lower with larger quantities There may be, as in five cases

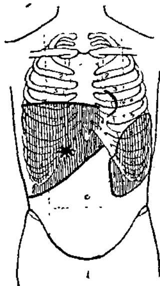


Fig 38—Liver abscess with splenomegaly (malarial) and advanced anæmia Recovery on emetine treatment.

Hæmoglobin, 40 per cent, red cells, 1,375,000 Grave blood changes, Wassermann reaction ++, * point of maximum tenderness

of the author's series, no increase of the leucocytes—a fact which may [illegible]

70 per cent, lymphocytes, 22 per cent, large mononuclears, 6 per cent, and eosinophils, 2 per cent Occasionally, however, eosinophilia is encountered, and may be, as in one case, as high as 60 per cent In these instances, some additional exciting cause may be present, for instance, asthma, so that the intrahepatic suppuration stimulated the already existing eosinophil response.

possibly a rigor. Pains in the shoulder are common. Pain and tenderness over the lower ribs with limitation of the respiratory movements are usually present, together with a cough, slight expectoration, and irregular fever.

Inquiry in a typical case will show that an accident followed upon

usually present. In a well-marked case there is an area of dullness clearly marked off from the resonance of the lung above, together with loss of breath-sounds and diminution of the vocal resonance When the abscess contains much gas a remarkable series of notes up to a tympanitic one may be obtained on percussion. In advanced cases the lower lobe of the lung may be so compressed as to give a zone of

of clear or purulent fluid in the pleural cavity above the subphrenic collection of pus The diaphragm itself may be perforated, so that the subphrenic and pleural abscesses connect with one another. Under these circumstances the mortality from subphrenic abscesses is 30–40 per cent

Generally speaking, a liver abscess is associated with a marked dull note over all the liver area, while the subphrenic has a resonant note of gas at one point at least.

Despite these symptoms and signs, it is notorious that the diagnosis of subphrenic abscess may present amazing difficulties as, indeed, Barnard's famous dictum "Pus somewhere, pus nowhere—pus under diaphragm" so freely admits This subject has been specially studied by S Wirssaladse (1937).

Aids to diagnosis of hepatic abscess.—Actual dysenteric symptoms are very seldom present in association with liver abscess, but usually some evidence of previous ulceration of the large intestine may be obtained by palpation of the abdomen, when infiltration of the sigmoid flexure (24 per cent. of cases) and of the cæcum (8 per cent.) may be elicited

Sigmoidoscopic examination may assist (*see* p 173), but it is not always possible to obtain evidence of ulceration of the lower bowel, as this is usually in and around the cæcum, far beyond the range of the instrument

Examination of the fæces.—When there are clinical evidences of hepatic abscess, the discovery of *E. histolytica* cysts in the fæces is of great confirmatory importance

Blood-examination. *Leucocytosis* —In association with pus formation within the liver, it is reasonable to expect an increase of the leucocytes, and usually there is a genuine increase; it varied from

toneum has been used with success in locating abscesses of the liver. By this method the organ is surrounded by a gaseous zone which renders its outline visible.

Radiography assists in the differentiation of liver abscess from subphrenic abscess, tuberculosis of the lung, and empyema.

Aspiration as an aid to diagnosis.—The most practical method of demonstrating the presence of an abscess is by aspiration—by drawing up liver pus into the exploring syringe Anatomical details have to be borne in mind by the operator At no point should the aspirating needle be inserted for a distance greater than 3¾ inches from the chest wall Beneath that zone lies the inferior vena cava, and fatal results have followed too vigorous an aspiration without due regard to anatomy The needle should be inserted, under local anæsthesia, at the most tender and prominent portion of the liver If, however, there is a definite bulging of an intercostal space in the axillary line, then that should be the point of election; sometimes, however, it may be advisable to select the posterior aspect of the thorax at the angle of the scapula In exploratory aspirations the needle should always be inserted in an upward and inward direction, i e, towards the nipple, the needle will then pass through the main structures of the liver, and will be likely to tap the abscess in the upper part of the right lobe. It will readily be seen that it is unsound to pass the needle in a strictly horizontal direction While the needle is entering the liver, traction should be made upon the plunger, in order that any pus encountered may enter the barrel of the syringe and be recognized

In acute cases liver-abscess pus is a characteristic chocolate colour, but in long-standing cases it may be thicker, of a gummatous consistency, and actually yellow. Very rarely can amœbæ be demonstrated in aspirated pus, the author has succeeded in doing so on only two occasions, though others have had better fortune, for S M Chen, G W Van Gorder and Y K Yuan (1931) found amœbæ in twenty-six out of forty cases The amœbæ usually appear in the pus at the end of aspiration, as they are situated actually in the walls of the abscess cavity The microscopic characteristics of the pus may be: (1) many disintegrating leucocytes, (2) hepatic cells undergoing fatty degeneration, and (3) cholesterin crystals. It is usually sterile on culture, but in longstanding cases streptococci and *Bacillus coli* may be present

H L Chung *et al* have described a novel method by aspiration,

or even months

Anæmia.—Anæmia is not a constant feature of liver abscess, unless absorption of septic material has proceeded for a considerable length of time. Grave anæmia with a reduction of the hæmoglobin below 80 per cent. has been encountered in eight cases, but in only one has the author observed changes so extreme as to resemble a genuine pernicious anæmia.

A Goanese steward was seen in October, 1928, with enlarged liver and spleen, the result of old standing malaria The hæmoglobin was reduced to 40 per cent and the red blood-corpuscles numbered 1,375,000, with normoblasts and alteration in the size of the cells Remarkable improvement of his blood-picture took place after aspiration of the liver abscess and emetine treatment. (Fig. 38)

Radiological evidence.—An X-ray examination may be extraordinarily helpful, or it may be the opposite The salient points to observe are fixation and limited movement of the diaphragm on the

seen by screening

In the author's series, doming of the diaphragm on the right side afforded an efficient help in one-third of the cases The picture showed stretching of the diaphragm, sometimes 2½ to 3 inches beyond the

laterally situated, becomes less acute, more nearly approaching a right angle (Plate X), but if the abscess is nearer the vertebral column, the angle is more acute. Serous effusions into the pleural cavity and

with a total

* The author recently treated a case in which a less opaque area in the liver substance delimited the actual cavity and formed an accurate guide to aspiration



Photo Dr G. Mather Cordiner

Radiograph of dome of diaphragm in amœbic abscess of liver

AMŒBIC ABSCESS OF LIVER

PLATE X

Liver-function tests.—*The value of biochemical tests in indicating involvement of liver function has been emphasized by A. F. Hurst.* In this connexion, the author's attempts to utilize the lævulose-tolerance and the bromsulphthalein tests have shown them unreliable.

TREATMENT OF HEPATIC AMŒBIASIS

Acute amœbic hepatitis (or hepatic amœbiasis) reacts very quickly to emetine injections given in the generally accepted dosage. The

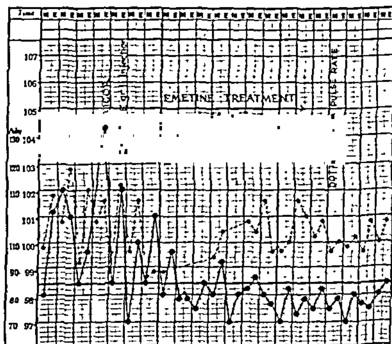


Chart 8.—Acute hepatic amœbiasis, showing immediate effect of emetine injections. The dotted line represents the pulse-rate.

[illegible] 2–3 grains. Subsequently (Chart 8.) [illegible] to anti-amœbic treat- [illegible] the administration of ipecacuanha powder. Aperients, such as the sulphates, should be used cautiously and the patient should be placed on a low dietary. *The liver is poulticed by hot fomentations and antiphlogistine,* and, if there is much pain, dry cupping may be resorted to or leeches may

be applied over the affected area. Ammonium chloride in 20-grain doses three times a day appears to have the effect of reducing it

There has been considerable controversy about the effect of emetine and E.B.I. in the treatment of *hepatic abscess.* In the author's opinion there are undoubtedly cases in which the physical signs of liver abscess and the accumulation of pus have disappeared upon intense anti-amœbic treatment; but this is by no means always the case The possible explanation of this will be given later

Can a liver abscess always be aborted or prevented from forming by routine treatment with emetine-bismuth-iodide? Since the adoption of E.B.I. and quinoxyl as the stock treatment for all cases of chronic amœbiasis, failure has once been recorded among the author's cases

This concerned a man of fifty-eight who had spent forty-two years in West and Central Africa In 1925 he had been operated upon for acute appendicitis, and he subsequently suffered from hepatitis and was said to have developed a liver abscess which was controlled by emetine injections. *E. histolytica* were found only once in the fæces, in January, 1934, when amœbic ulcers were demonstrated in the bowel by sigmoidoscopy During the nine years he had suffered from time to time from febrile attacks which [illegible]

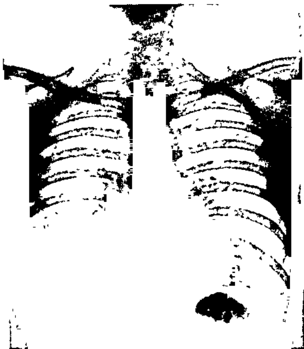
E B I. and quinoxyl lasting twelve days

On his return to Rhodesia he remained well for a year, then the febrile bouts recommenced, and in October, 1935, he returned to have an exploratory laparotomy performed for suspected cholecystitis In November, 1935, a chronic intralobar hepatic abscess the size of an apple was found in the posterior part of the right lobe of the liver, where it was very difficult to locate and approach It was drained, and four ounces of pus escaped Convalescence lasted eight weeks, but was retarded by the intervention of an attack of amœbic dysentery with blood and mucus in stools containing numerous active *E histolytica*, and later by a *B coli* bacilluria The dysentery was controlled by a further course of E B I and quinoxyl and the bacilluria by mandelic acid treatment The patient finally recovered and has remained free from any symptom of amœbiasis ever since

When rigors are present or when there are signs of bulging or œdema, medicinal treatment is of little value, and steps must be taken to aspirate pus from the liver

Aspiration.—Aspiration of liver pus by means of Potain's aspirator has received much support It must, however, always be preceded by preliminary aspiration Local anæsthesia (2-per-cent novocain) is usually sufficient, but general narcosis is advisable in nervous subjects A medium- or full-sized aspirating needle is used, as the pus may be too thick to flow through a cannula of smaller bore Yellow serous fluid suggests a pleural exudate, especially when fibrin is present, and may indicate an underlying hepatic abscess Sometimes, even





Photos: Dr G Mather Cordiner.

Left, Pleural effusion into right pleural cavity, associated with liver abscess. After aspiration, the pleural effusion disappeared and the site of the abscess was marked by a gas vesicle.
Right, Transdiaphragmatic rupture of liver abscess into right lung, with expectoration of liver-pus.

AMŒBIC ABSCESS OF LIVER

PLATE XI

days before aspiration, as this procedure definitely lessens the risk of

A ship's engineer was seen in November, 1932 He had suffered four months previously from amœbic dysentery, and had been treated on board ship as

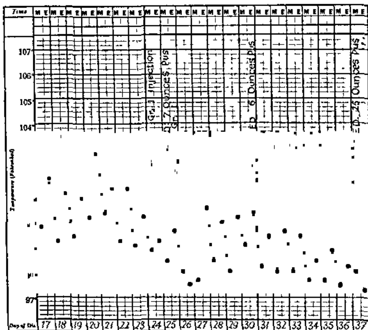


Chart 9.—Amœbic abscess of liver, to show effect of the combined aspiration and emetine treatment. The result was successful.

a case of pleurisy, on account of right sided pain. The signs and symptoms of liver abscess were fairly definite and were confined to the liver and base of the right lung, shoulder pain was also marked. The X ray examination

when no pus is found, great improvement follows the aspiration of several ounces of blood from the liver (*hepatic phlebotomy*).

In 1902 Sir Leonard Rogers advocated repeated aspiration of the hepatic abscess, and injection of quinine in solution as an amœbicide.

The records of the British Army in India in the closing days of the last century are very impressive. Out of 2,661 cases treated by open operation, the mortality was 56.7 per cent. This was before aspiration methods had been generally adopted. Since that time, out of 111 cases, collected from various sources, which were treated by aspiration alone, the mortality has been shown to be less than a quarter of that figure.

The advantages of using Potain's aspirator are many; the death rate has been reduced considerably; the shock to the patient is negligible, and several pints of pus may be evacuated When anti-amœbic treatment is instituted, recurrence, in the majority of instances, does not take place. When pus has been found by exploratory puncture, the aspirating needle is inserted along the same track and pus will flow when the stop-cock of the exhaust bottle is turned Should the pus prove to be too thick for aspiration it may be diluted by injection of weak eusol solution into the abscess cavity. The method is so simple that it may be practised in the patient's room in the absence of the facilities offered by an operating theatre.

Sometimes almost incredible quantities of pus are aspirated. The author has frequently obtained 40–60 oz., but in one reported by A. C Alport and F Ghahoungui 3,500 c c (120 oz.) were removed by one aspiration The total amount was 8,100 c c. (270 oz.) in four aspirations The liver therefore showed itself capable of accommodating nearly one and a half times its volume of pus without rupturing

Usually an effusion of serum takes place into the abscess cavity immediately after the aspiration, and the swelling and pain thus produced may give
pus, likewise a p
sometimes occurs
is painless
The a
election.
but in
performe
punctures by this method, but unless the liver substance is actually lacerated, there appears to be little danger Whenever possible, 3 or 4 grains of emetine should be injected hypodermically three or four

500 c c of pus, open operation was performed and a tube inserted into the abscess cavity Active *E histolytica* were found in the pus, but there was no response to treatment with E B I (19 grains)

The recovery of this case after admission to the Hospital for Tropical Diseases on March 19, 1931, was due to the establishment of free drainage On re opening the wound in the seventh intercostal space in the mid-axillary line, 10 ounces of claret like pus were evacuated, 1½ inches of the eighth rib were resected, and the cavity was explored and thoroughly washed

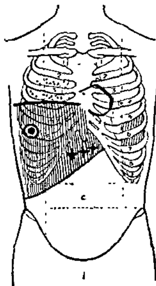


Fig 39—Liver abscess of anterior surface of right lobe, South African Infection.

Signs at base of right lung, no *E histolytica* cysts in fæces, leucocytes, 24,000 Open operation, 40 fl oz. of pus evacuated, secondarily infected with *Bacillus coli* ⊙, site of abscess, +++, maximum tenderness.

out with normal saline A rubber drainage-tube was inserted and the Carrel Dakin method of continuous drainage [illegible]

Necrosis of one or more ribs in the vicinity of the drainage-tube is a not uncommon event after operation for hepatic abscess Lecomte (1913) has described six cases and thinks that this complication is more frequent in those instances where the abscess has been opened without resection of a rib, and that it is caused by insufficient drainage,

The open operation.—Only occasionally at the present time has resort to be made to open operation and drainage of liver abscess. In longstanding cases the pus may be so thick, and the necrotic tissue in the wall of the cavity so abundant, that the only means of evacuating it is thorough drainage and irrigation by the Carrel-Dakin method. Secondary infection is the most important indication for this method

A. C. Alport and F. Ghalioungui (1939) think that the modern practice should be to aspirate the abscess before operation, stain a smear of pus, and examine for bacteria and, when *B. pyocyaneus* or other organisms are present, to give sulphonamide 2 grm. for 10 days, with injection of soluceptacine into the abscess cavity

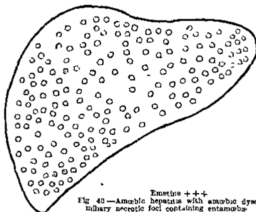
present they are divided, and sinus forceps are directed along the needle and pushed through to the abscess; the blades are opened after withdrawal of the needle. A suction apparatus minimizes the risk of soiling.

time. The two-stage method is

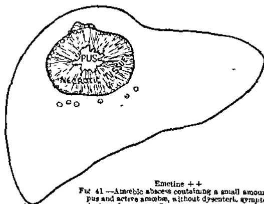
owing the necessity of obtaining operation.

In December, 1930, he was admitted to a London hospital, where enlargement of the liver was recognized, also involvement of the base of the right lung. The leucocytes numbered 14,758 After a preliminary aspiration of

action in acute amœbic hepatitis which occurs in the course of amœbic dysentery In amœbic hepatitis numerous small necrotic foci containing "nests" of amœbæ form in the liver (Fig 40) It is reasonable to suppose that emetine therapy extirpates these and that the surrounding necrotic tissue is absorbed. These considerations are based upon the observed fact that the alkaloid—emetine—has a selective action upon the trophozoites of *E histolytica*, while E B I exerts a special action upon cysts



Emetine +++
Fig 40—Amœbic hepatitis with amœbic dysentery, miliary necrotic foci containing entamœbæ Action of emetine very effective.



Emetine ++
Fig 41—Amœbic abscess containing a small amount of pus and active amœbæ, without dysenteric symptoms. Action of emetine effective

Figs. 40, 41—Diagrams to illustrate the formation of amœbic abscess of the liver.

or, it may be, by pressure of the drainage-tube. The necrosis usually affects the anterior part of the ribs and their cartilages.

Treatment after operation.—For the first two days after a liver abscess has been opened, the discharge is considerable, and the dressing may have to be changed frequently. Very soon, however, should the case do well, the discharge diminishes, and the dressing requires renewal every other day, or every three or four days. During the first week the drainage-tube, provided it be acting efficiently, should not be disturbed, more particularly as it may be difficult to replace. Later it may be removed and cleaned and, when discharge has practically ceased, cautiously shortened. *It is a great mistake to*

is serious and it may be fatal

Should an abscess, on being opened, be found to be secondarily infected, or should it become so, it must be flushed out daily with a weak non-mercurial antiseptic, and a counter-opening made if necessary. Continuous drainage by the Carrel-Dakin tube method, and daily eusol irrigation is often very successful.

After a liver abscess has been opened and is draining well, the temperature rapidly
fever persist, it is to
there are other absc
arisen If another a
aspirator and drained

It is advisable to give emetine hypodermically in 1-grain doses both before and after the operation, and to continue to exhibit it for a fortnight

If any symptoms of hepatic inefficiency due to extensive destruction of liver tissue are noted, the presence of diacetic acid or a high ammonia coefficient in the urine should be an indication for the oral or rectal administration of glucose and sodium bicarbonate, or, in some cases, for intravenous injection in 5- to 10 per-cent. solution

After evacuation, a Carrel's tube is passed inside the larger drainage-tube and irrigation with Dakin's solution is carried out, by means of a large glass syringe, at two-hourly intervals, for nineteen days A preparation containing ferments (Enzymol, Fairchild), half an ounce to an ounce of water, is useful for injection into the abscess cavity for dissolving adherent sloughs

Indications for emetine treatment.—It is necessary that some hypothesis be formulated as to the *rationale* of these various methods of treatment. Most authorities recognize that emetine has a selective

combined with emetine therapy is effective The amount of pus is too large to be absorbed, and the amœbæ in the abscess cavity are vulnerable to the action of the emetine

In the final stage, the abscess cavity has grown to a large size and the active amœbæ have died out, because conditions are unfavourable to their further multiplication A similar process takes place in gummata of the liver and in tuberculosis, in which diseases also the causative organisms eventually disappear

As a rule, in longstanding amœbic abscesses secondary infection

October, 1931

Date 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2 3 4 5

106

105

Chart 10 —Fatal case of amœbic abscess of the liver. Rupture into the right lung. Death from streptococcal septicæmia. Failure of emetine and aspiration therapy.

[illegible]

and perforated to afford efficient and continuous drainage. (Fig 43)

Prognosis of Hepatic Abscess

Under modern conditions, with early operative interference and with emetine and E B I therapy, the prognosis is good in cases of single abscess. In multiple abscesses, however, or in a single abscess if it is loculated, it is by no means so good, and if there are more than two or three abscesses, it is usually hopeless

If partial rupture into the lung takes place, there is danger that the original abscess cavity may become infected with streptococci, and

The next stage in the formation of a liver abscess, which may be termed the early suppurative stage, is less acute. Here the necrotic tissue, which has been liquefied by the action of the amœbæ, is sterile (Fig. 41). The amœbæ living in the actual abscess cavity are still in an active state of multiplication and are vulnerable to the action of emetine. Small intrahepatic abscesses yield rapidly to emetine

containing active amœbæ (Fig 42.) It is at this stage that aspiration

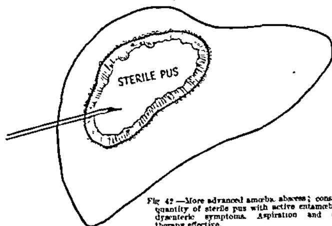
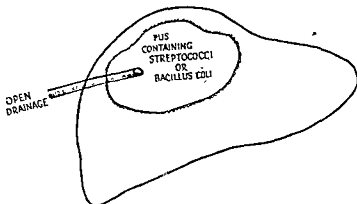


Fig 42 —More advanced amœba abscess; considerable quantity of sterile pus with active entamœbæ. No dysenteric symptoms. Aspiration and emetine therapy effective.

Figs. 42, 43.—Diagrams to illustrate the formation of amœbic abscess of *the liver.*



CHAPTER XV

AMŒBIASIS (*continued*): RARER AMŒBIC LESIONS

AMŒBIC ABSCESS OF THE LUNG (PULMONARY AMŒBIASIS)

As a general rule, amœbic abscess of the lung is secondary to abscess of the liver, but primary pulmonary amœbic lesions have rarely been described Usually they are single, but they may be small and multiple. The lower lobe of the right lung is the part usually involved, and the diaphragm becomes adherent to the lung as well as to the liver. Rupture takes place into the bronchus and the pus is then expectorated

Microscopic pathology —The inner surface of the abscess wall consists of a zone of necrotic material containing histolysed lung cells, amœbæ, a few polymorphonuclear leucocytes, and many lymphocytes

In most cases of amœbiasis in which the lung is affected, direct extension of a previously existing hepatic abscess through the diaphragm can be proved to have taken place Rupture of an unrecognized

amœbiasis—may simulate bronchiectasis or unresolved pneumonitis (Plate XI, right, facing p 235)

The author has records of instances of this complication, in two of which the diagnosis of tuberculosis had originally been made

that eventually a streptococcal septicæmia may result. (Chart 10) The following case illustrates this point :—

A mining engineer had suffered for nearly thirty years during his residence in India from periodical attacks of diarrhœa, but the first inklings of a liver abscess were noted on July 13, 1931, when he fell from a ladder on his left [illegible]

the right lobe of the liver; one was healed and one in the process of granulation, but the third, which had not been touched by any of the operative [illegible]

The question of return to the tropics after recovery from liver abscess is a matter that frequently has to be decided. If a relapse of the amœbic abscess has occurred during treatment, or if very considerable *damage to the liver tissue has taken place, the patient should remain* in a healthy and temperate climate; but there are many instances of patients who have enjoyed permanent good health in the tropics after recovery from liver abscess Before giving permission for the patient to return it must be ascertained, by repeated sigmoidoscopy and examinations of the *fæces, that the bowel is thoroughly cleared* of amœbic infection Through neglect of this precaution, re-infection of the liver from the bowel may occur. Recurrences of liver abscess have been known after periods as long as from five to seven years from the formation of the first.

[illegible]

increases, or if the patient continues to lose weight, an attempt should be made to reach and drain the abscess from outside, especially if there is no response to medicinal treatment after full doses of emetine and ipecacuanha If the temperature remains normal, the pus gradually decreases, and the body-weight is maintained, operation is unnecessary, or at all events should be deferred

[illegible]

Primary pulmonary amœbiasis.—In a case of primary pulmonary

[illegible]

and in microscopic section the organisms were seen penetrating the wall of a pulmonary artery

Colin in 1873 described ten abscesses of the lung which were secondary to a thrombosis in the liver, and in a case reported by Moxon the liver abscess had actually burst into a subhepatic vein and then spread to the lung In primary pulmonary amœbiasis, the probable route by which the amœbæ gain access to the pulmonary circulation is, as suggested by C H Bunting in 1906, by direct embolism into the lung through the circulation from the colon In Bunting's case firm consolidated nodules were found in the lung, and in each entamœbæ were demonstrated in section

In another case, described by Opie in 1901, a large amœbic abscess was

[illegible]

present Loison reported a similar instance, and suggested aspiration of the pus The abscess cavity was outlined by means of a radioscopic screen The same patient subsequently developed a hepatic abscess. J W S. Macfie (1920) found at autopsy, an amœbic abscess of the lung in association with a

[illegible]

X-ray examination may not reveal any evident lesions, but B A

in India and had recently returned to England on leave. The signs

two days she developed signs of pleurisy at the base of the right lung; days later there was high fever with hæmoptysis and expectoration of b stained, frothy pus, accompanied by acute diarrhœa. X-ray examin

E histolytica cysts were found in the fæces and he had a leucocytos 20,000 On appropriate treatment with emetine and ipecacuanha a r recovery took place This case was notable in that the skiagram showed

There are various points to be noted in connexion with the diagn of transdiaphragmatic rupture of liver abscess. Hiccough is a uncommon accompaniment. Chocolate-coloured liver pus is usu

in large amounts at periodic intervals Lying on the sound lung up irritation, while relief is obtained by turning to the affected si Some assistance in diagnosis can be obtained from the microsco appearances of the expectorated pus, which usually contains Charc Leyden crystals, the remains of liver cells, and epithelioid cells deri from the lung Sometimes fibres derived from the muscles of diaphragm may also be recognized

hitherto been realized, their recognition having been prevented by the difficulty in obtaining evidence of associated amœbiasis

re and
use was
paper
They
were single, and affected the cerebrum, but in one case the cerebellum

It is by no means certain that all the recorded cases are examples of amœbic infection. According to F. L. Armitage, who collected

of the patients has recovered

The abscess is described as being generally single and as occurring with equal frequency on the right and left side; bilateral abscesses have been found on six occasions. In recent acute cases there is no resulting pyogenic membrane, but in those of long standing there is a tendency to formation of a cyst-wall.

The solitary case described in recent years is that recorded by T. D. M. Stout and D. E. Fenwick (1918). The patient was operated on for a liver abscess, and in the discharge from the cavity active

The differential diagnosis has to be made from cerebral malaria, metastatic septic abscess, caseating tuberculosis of the brain, cerebral gumma, and actinomycosis.

The disease is rapidly fatal, death in the recorded cases taking place on the sixth to the eighth day from the onset of headache.

Amœbic abscesses of the spleen, epididymis and penis.— L. Rogers has described several cases of abscess of the spleen in his records of autopsies in Calcutta, all secondary to amœbic abscesses of the liver. O. Jacob (1911) collected fifteen cases of hepatic compli-

dilatation of the ducts, in which masses of spermatozoa and numerous amœbæ were demonstrated.

H. E. Shih, J. K. Wu, and V. T. Liеu (1939) described an amœbic ulceration of the penis, of five months' duration, healed by emetine injections.

Dormer and J. Friedlander (1941) state that the radiographic appearances may resemble tuberculous infiltration or bronchopneumonic consolidation.

So far, there are no authentic instances of amœbæ having been demonstrated in the sputum, although various observers have described bodies which they thought might be dead organisms, but which probably were the large epithelioid cells usually present in inflammatory pulmonary conditions.

Three cases of primary pulmonary amœbiasis which have occurred in the author's practice are described below. All three responded in a dramatic manner to emetine and ipecacuanha therapy. It will be noted that the diagnosis of this curious condition must be based upon the previous history of intestinal amœbiasis, the leucocytosis, and lasting response to emetine therapy

The first case was that of an ex-soldier who had suffered from amœbic dysentery in 1918, and was admitted to hospital in March, 1921. He was ill and emaciated, and his main symptoms were acute pain in the lower chest on the right side, accompanied by cough, fever, and respiratory distress. Profuse purulent sputum, without hæmoptysis, was expectorated, and an intermittent pyrexia varying between 101° and 102° F. with nocturnal sweats, and a leucocytosis of 14,000 were present No clubbing of the fingers was noted. A patch of dullness 4 inches in diameter was found below the angle of the right scapula, with bronchial breath sounds and occasional crepitations Later, similar broncho-pneumonic areas became apparent in the lower lobe of the left lung. The sputum contained numerous pus and large epithelioid cells. No evidence of liver involvement was found The probable diagnosis appeared to be tuberculous broncho-pneumonia but, as no improvement took place after a month in hospital, emetine injections (1 grain) daily, together with 10 grains of powdered ipecacuanha, were instituted. There was immediate improvement; the temperature became normal, and the patient recovered and regained 28 lb. in weight.

An ex-soldier from Mesopotamia had suffered from amœbic dysentery with numerous relapses, and had been treated in hospital Re-admitted in May, 1921, fourteen days later he commenced to suffer from rigors, together with bronchial pneumonic consolidation of the lungs, nocturnal perspiration, [illegible]

[illegible]

temperature fell immediately and there was a gain in weight of [illegible] X-rays afforded little assistance in the diagnosis

It is probable that these cases are much more frequent than has



Fig. 44.—Amœbic granuloma and ulceration of the abdominal parietes surrounding colostomy.



Fig 45.—Amœbic granuloma and ulceration of abdominal parietes surrounding colostomy. Appearance after injection of 8 grains of emetine.

Amœbic infection of the skin and other tissues.—It appears that under certain circumstances invasion of the skin by *Entamœba histolytica*, producing extensive destruction and sloughing of the tissues, may take place in the vicinity of a discharging amœbic abscess of the liver, or in immediate proximity to the bowel.

L. Tixier, M. Favre, E. Morenas, and C. Petouraud (1927) have described in minute detail a peri-anal lesion in a man suffering from chronic dysentery. It had been present for six years, but healed rapidly after emetine injections. In the pus entamœbæ were found. Examination revealed microscopic, punched-out ulcers of the epidermis, and of deep-seated colonies of amœbæ.

M. F. Engman and H. E. Meleney (1931) found amœbæ in ulcers of the skin and deeper tissues of the abdominal wall. One ulcer was secondary to an operation for resection of a portion of the colon involved in amœbic ulceration; the other followed drainage of an amœbic abscess of the liver. Clinically, the skin lesions showed a rapidly spreading ulcerative process and a border presenting irregular outline. There was extreme pain on pressure, and the floor of the ulcer was composed of granulation tissue covered with débris and pus.

S. F. Ngai and C. N. Frazier (1933) made a careful and complete survey of the literature of this subject since 1891, together with a ... They ... he best ... patient suffered from a tumour in the right lumbar region which discharged liver pus, and from that time an ulcer developed in the mid-axillary line, which ... stained sections of ... metine therapy the ...

A case of ... which ...

was undoubtedly ... had served fifteen years previously in the Army in India and had

R. V. Rajam and P. N. Rangiah (1939) have described amœbic anal ulceration and stricture of the anal orifice, which was cured by emetine and E B I

The histopathology of these lesions demonstrates the destructive action of the amœbæ; once they have reached the epithelium, the cells are progressively dissolved, so that punched-out ulcers are produced There is a sero-fibrinous and cellular exudate which becomes necrotic on account of a lytic action of the amœbæ

Skin lesions produced by *E histolytica* have also been recorded by A Carini (1912), M F Engman and A S Heithaus (1919), Van Hoof (1926), and S. Crawford (1933)

Urinary amœbiasis.—Numerous observers have reported infection of the human bladder by *Entamœba histolytica* and appearance of this organism in the urine The evidence in the great majority of cases is very unsatisfactory, large inflammatory cells from the bladder wall, or from the prostate, often being mistaken for *E. histolytica*. In the author's experience *E histolytica* cannot survive in urine for any length of time Considerations such as these are entirely lacking from the many uncritical papers which have appeared on this subject, especially one by K D Manohar.

E. histolytica cysts in the fæces, he had never suffered from diarrhœa or "dysentery." The primary lesion appears to have been a perirectal abscess. A left iliac colostomy was performed. In spite of irrigations, ulceration spread relentlessly to the perineum, sacrum and also on the abdominal wall round the colostomy wound. The patient was extremely ill with hectic fever and tachycardia. There was an enormous ulcerating cavity which had destroyed the rectal floor. Response to emetine was instantaneous. After 8 grains the cavities had granulated up and the amœbic infection was cured by E B I and quinoxyl. Thiersch grafts were subsequently applied.



Fig. 46.—Section of amœbic skin granuloma, showing invasion of subdermal tissues by *Entamœba histolytica*

C. H Hsu (1937) in Peiping, China, described a series of fourteen cases, and in his opinion the condition is by no means rare. Amœbiasis cutis occurs chiefly as an unsuspected secondary infection of papillomata, usually of the anal region The lesions generally take the form of characteristic punched-out ulcers, implanted upon peri-anal papillomata, in the urethra, on condylomatous growths of the anus and vulva, even situated in the cervix, on carcinomata of that region, as well as on papillomata of the labia majora and minora These ulcers are aptly termed by the French workers, Tixier et al (1927), "*porodermie amibienne*" The lesions produced are fundamentally similar to those found in the intestine.

R V. Raijam and P. N Rangiah (1939) have described amœbic anal ulceration and stricture of the anal orifice, which was cured by emetine and E B I

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Usually the presence of a fistulous opening between the bowel and the bladder causes the parasite to appear from time to time in the urine In 1911 C F Craig recorded a case in which *E histolytica* were found in the urine of a patient suffering from a fistula between the bladder and an ulcerated area in the intestine

CHAPTER XVI

BALANTIDIASIS, GIARDIASIS, FLAGELLATE DIARRHŒA, INTESTINAL COCCIDIOSIS, MALARIAL AND LEISHMANIAL DYSENTERIES

BALANTIDIASIS

Synonyms.—Balantidiosis; Balantidial dysentery; Ciliate dysentery.

For the past fifty years it has been recognized that a form of diarrhœa, or dysentery, may be caused by a ciliate protozoan—*Balantidium coli* This is a common parasite of the domestic pig and of monkeys, and in

described by P H Malmsten (1857). He knew the protozoon as

H. Ziemann (1925) with special reference to clinical and pathological findings. F Pritze (1928) has summarized much of the knowledge of this subject in a thesis for Berlin University.

Human cases ha
with it, i e , in
experiments dire
Casagrandi and P. Barbagallo (1895), who tried to infect themselves by swallowing suitable material, were unsuccessful

A. Sevra (1931), in Porto Rico, records that in over 5,000 stool

Fig. 47.—*Balantidium coli* in fæces.
(Photomicrograph, Dr H K Giffin, Amer Miss Hosp, Assiut, Egypt)

examinations, *Balantidium coli* was seen only four times, and that in only one were dysenteric symptoms noted

Geographical distribution.—Cases have been recorded in the following localities —

Europe .	[illegible]
Asia	Siberia (Port Arthur), China (Tsingtau, Trembur) Philippines, Siam, India (Assam), Marianne Islands Cochin China, Sandwich Islands, Andaman Islands
Africa	Egypt (Alexandria), Sudan
North America	Seven in mental defectives in S Carolina (M D Young, 1939), two from Tennessee (H E Meleney)
South and Central America	Brazil (Rio de Janeiro), Porto Rico, Cuba

E Brumpt (1909) summarized the distribution of this parasite, and Dopter (1924) has enumerated 232 cases, among whom were 143 Europeans D L Mackenzie and H Bean (1938) recorded the first case in Great Britain in a mental patient

Pathology—Fatal infections are found in man as well as in monkeys. The researches of M Askanazy (1903), R. Strong and W E. Musgrave have shown that the balantidia penetrate into the bowel-wall in the

same manner as *E. histolytica*, and in the blood-vessels of the mucosa and submucosa
hyperæmia of
swellings, with
usually blackish: recent ones irregularly shaped with undermined edges
ing the ,
(Fig. 48)
ferment



Fig. 48.—Microscopic section of the large intestine in human balantidiasis, showing the position of the balantidia in the submucosa.

Histologically, there is little to distinguish the ulcerated bowel from amœbic ulceration, but the organisms have been found by

Symptomatology.—The symptoms produced by the balantidium in man are, as far as we know, almost indistinguishable from those of amœbic dysentery In balantidial colitis there is colicky pain, slight [illegible]

[illegible] change, there is no leucocytosis and the polymorphonuclears number 70 per cent

This infection has been observed to persist, on an average, from four to fifteen years

Treatment —From experimental work, E. L Walker (1913) concluded that organic compounds of silver were most effective in eradicating the infection, but in actual practice these preparations have not been found useful

At present therapy is purely empirical The following drugs have been employed thymol as in ancylostomiasis, calomel, carbolic acid in pills, extract of filix-mas, methylene blue, ipecacuanha, emetine; quinoxyl; oil of chenopodium, stovarsol and santonin Enemeta of iodine solution 1 10,000 and tannin 1 1,000 with 10–15 drops of tincture of opium, and of quinine have also been used

N. Kipschidse (1928) reports that during four years, twenty-two cases of *Balantidium coli* infection have been treated in hospital in Tiflis, of which three came to autopsy. He found that emetine injections in large doses—0 05–0 06 gramme in fifteen to twenty injections—gave the best results Good results from this drug are also reported by A Luger and L Korkes (1928).

E C. Cort (1928) reports that, following the suggestion of C. W. Mason (1919), he treated twelve cases in Siam by enemata of 15 c c of oil of chenopodium in 150 c c of olive oil, and all patients remained free from *Balantidium coli* thereafter. In one case a second treatment within twenty-four hours of the first brought about symptoms of chenopodium poisoning

H F [illegible]
on two [illegible]
Gupta, a [illegible]
by stov[illegible]
4 grams

D Yered tried a new remedy, Carobinase, a watery extract of *Jacaranda decurrens*, 25 grammes in 500 c c of hot water, as a rectal lavage for three weeks There was great improvement in the patient's condition, and a definite cure was established

A correspondent reports that in his case, in Egypt, all the parasites

disappeared from the stool after three treatments of carbon tetrachloride of 1 drachm (1 teaspoonful) each

D. L Mackenzie (1938) treated his English case satisfactorily with 2 pints of methylene-blue solution by enema.

A Westphal (1939) employed Acranil—the hydrochlorate of acridine—in one case and found that it caused apparent disappearance of the parasites from the fæces

GIARDIASIS

Synonym.—Lambliasis.

Of the protozoan flagellates that inhabit the bowel of man, *Giardia intestinalis* has the best claim to be regarded as pathogenic, though authorities are by no means agreed upon this subject.

Ætiology.—This flagellate was first seen in 1681 by Leeuwenhoek, through his primitive microscope, in his own excreta. It was rediscovered by Lambl in 1859 and was known for a long time as

Children appear to be more commonly affected than adults; F. W. Bach and K H Kiefer found that, in a district in Germany where 25–27 per cent of the children were infected, only 9.7 adults were in a similar condition

Some authorities consider that the number of this parasite in the fæces depends upon the diet of the host, for R Hegner (1924), and later C. D. de Langen (1927) found that it disappeared from the intestinal canal of infected animals fed upon meat The parasite has been found by intubation in the duodenal juice (E. Libert and G. Lavier, 1923), but there appears to be no conclusive evidence that it is in any way connected with disease of the biliary apparatus According to

en,

to

and

occasions demonstrated by intubation, but not in the excised gall-

The morphology of *Giardia* is described in the Appendix (p. 542).

Geographical distribution.—The following are the countries of origin in a series especially studied by the author. The cases have been derived from almost all over the world: India (3), Ceylon (5), [illegible] (1), South Africa (2), Cape Verde Islands (1), [illegible]

Pathology.—Numerous investigators have brought forward evidence of the pathogenicity of this parasite and have contributed the following information. (*a*) It is found in its active state and in the largest numbers when the stools are liquid and diarrhœic. (*b*) In the early stages symptoms of gastro-enteritis are present, while in the chronic stages stools have characteristic features and contain [illegible]

[illegible] that sooner or later it must give rise to symptoms. At first it colonizes the duodenum and may beset the mucous membrane so closely that [illegible]

[illegible] months old. (*f*) G. Tenso, in Italy, has divided the cases of this infection into three types: (1) non-intestinal, associated with anæmia and nervous disorders, (2) intestinal, with signs of entero-colitis, and (3) acute, with dysenteric symptoms. In the acute stage, when active stages are present, the stool is definitely dysenteric in character. (*g*) R. Deschiens (1923) believes that this parasite is pathogenic to children in France. C. M. Wenyon, in his review of this subject, concludes that it is difficult to avoid the impression that the mucus in the stools is produced from that part of the intestine where [illegible]

With these latter views the author has been in agreement for a number of years, and he has had the opportunity of studying twenty-six cases in adults in hospital. Most of the patients were admitted with a history of recurrent dysenteric attacks, and some, on account of the large, pale, ochreous stools they were passing, were suspected of sprue.

Arguments against the pathogenicity of this parasite are based

largely upon the very considerable number encountered who, with numerous cysts in their fæces, do not complain of intestinal symptoms.

It is a disturbing fact that *Giardia* is capable of multiplying in the human intestine without appearing either in the active phase or in cystic form in the excreta. Thus, J. McGrath, P. T. O'Farrell, and S. J. Boland (1939) have reported a case in which symptoms suggesting idiopathic steatorrhœa, rapidly progressing to death, became apparent after cholecystectomy. The duodenal contents contained numbers of active *Giardia intestinalis* but, in spite of intensive search, none of the flagellates or their cysts were seen in the fæces. At autopsy the mucous membrane of the duodenum and jejunum was attenuated, the villi

cholecystectomy
No active *Giardia*
was re-examined

two years afterwards with the same results.

Incidence.—In the author's series there were twenty-four cases in men and two in women. No infections in European children from the tropics were observed, though undoubtedly they do occur.

Symptomatology.—The duration of the symptoms varies from one month to over ten years. The main complaint is of initial diarrhœa of a lienteric character, followed by a more or less chronic condition of intestinal disturbance. Flatulence is almost invariably present. *Acute exacerbations occur with diarrhœa and passage of* a considerable quantity of bile-stained mucus.

The frequency with which the different symptoms were noted in the author's series was as follows: flatulence in fifteen; abdominal distension in four; lassitude in twenty-two; anorexia in eighteen; vomiting in one; alternate constipation and diarrhœa in twenty-four; chronic constipation in two. *Abdominal pain* varied in intensity from

fifteen, *in the hypogastrium in one, over the cæcum in one, generalized* in three, and was more pronounced during the night than the day. In nine cases the large bowel was spastic and palpable, especially the sigmoid colon, but in these there was a previous history of dysentery of the amœbic type. In three there was an associated enlargement of the liver.

Stools varied in number from two to eight per diem. The dejecta were pale or yellow, but, as a general rule, even more offensive than sprue stools, which they otherwise resemble. Usually they were of normal size This description agrees in the main with the findings [illegible]

were free and encysted forms of *Giardia* associated.

Previous alimentary illnesses —Eight cases in this series had a previous history of amœbic, and five of bacillary dysentery Three had previously suffered from typhoid, and in two chronic indigestion, [illegible]

a coincident infection with *Ascaris lumbricoides*, and in another with subtertian malaria

The following is a description of a typical case of giardiasis mimicking sprue —

[illegible]

Giardiasis in children.—P. Véghelyi (1938) finds that infection by this parasite in children is symptomless or causes insignificant complaints in only one quarter of cases. In the majority, infection is followed by acute symptoms which may become chronic and lead to anæmia, which in turn impedes normal development All these symptoms may be explained by impeded resorption capacity of the intestinal tract. The following complaints have been noted: anorexia, headache, diarrhœa and indefinite abdominal pains.

Diagnosis [illegible]

Treatment.—The treatment of giardiasis was unsatisfactory before

1937, but the specific action of atebrin, or quinacrine, as foreshadowed by L. Brumpt (1937), which banishes both the active parasite and its cysts from the fæces, has been confirmed from a number of French, German, Russian, Italian, Spanish and South American sources (A list of references is provided in the bibliography). Atebrin acts equally well when given by the mouth or injected in a soluble preparation, atebrin musonate.

The course consists of 0 1 grm. three times daily for 5–7 days. For children of ten years or more 2 tablets daily, one at midday, the other at night for 4–5 days (Garin and Maffi) P. Martin (1937) considers

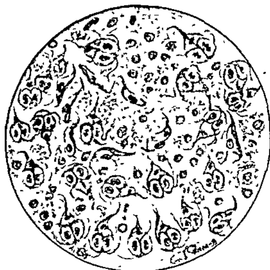


Fig. 49.—Mucous exudate in a case of giardiasis, showing active flagellates disposed like fish in a stream.

that it may be necessary to repeat the course E. N. Votrina, in a series of 25 cases, finds atebrin effective in children, especially when there are symptoms of enterocolitis, but less so when there are associated symptoms of cholecystitis.

parasites.

German and Scandinavian workers write enthusiastically about *Acranil*, the hydrochlorate of a new acridine compound, in doses of

FLAGELLATE DIARRHŒA*

For some considerable time it has been questionable whether all the species of flagellates which have been described in the intestines of man are to be regarded merely as harmless commensals, or whether, on the other hand, they may be either primarily or partially pathogenic. The question does not admit easy solution. It cannot even be settled by

cases of chronic bacillary dysentery and of sprue, and it should suggest to the clinician that there may be at the same time some other primary

the unhealthy.

One cogent point in favour of those who hold that flagellates can

* For a description of the morphology of the intestinal flagellates, see Appendix (p. 542)

1937, but the specific action of atebrin, or quinacrine, as foreshadowed by L. Brumpt (1937), *which banishes both the active parasite and its cysts from the fæces*, has been confirmed from a number of French, German, Russian, Italian, Spanish and South American sources. (A list of references is provided in the bibliography). Atebrin acts equally well when given by the mouth or injected in a soluble preparation, atebrin musonate.

The course consists of 0.1 grm three times daily for 5–7 days For children of ten years or more 2 tablets daily, one at midday, the other at night for 4–5 days (Garin and Maffi) P. Martin (1937) considers

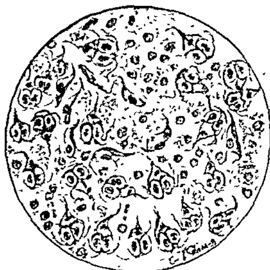


Fig. 49.—Mucous exudate in a case of giardiasis, showing active flagellates disposed like fish in a stream.

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J. Love and G B Tayloe (1940) have had remarkable results in four cases in which symptoms and parasites disappeared after a single course of atebrin The author has verified these experiences in a series of [illegible] J T Culbertson

parasites.

large numbers and in an active free state, in association with diarrhœa and dysenteric symptoms, indicates an abnormal condition of the mucous membrane of the large intestine which has previously under-

[illegible]

flagellates must, therefore, be looked upon as secondary invaders, and means must be taken to eradicate them, if possible

Additional evidence of their association with dysentery is afforded by the fact that, in chronic diarrhœas of indigenous origin occurring in Europe where bacillary infections are very exceptional, flagellate diarrhœa is not usually met, whereas it is a very common state in those tropical countries where these bacillary infections abound

Treatment —There does not appear to be any specific treatment

[illegible]

action upon *Trichomonas intestinalis* Neither [illegible], [illegible], nor acriflavine have any influence upon any intestinal flagellates other than *Giardia intestinalis*

INTESTINAL COCCIDIOSIS

[illegible]

the same year by C M Wenyon

exists otherwise than as a saprophyte. This parasite has also ... uncommonly found in the urine ... is capable of penetrating the ... gynæcological circles *T. vaginalis* ... tative vaginitis and leucorrhœa ... dition in cattle, producing abortion Special measures, such as stovarsol "vaginal compound S.V.C.," *eliminate the infection* The vagina is douched with normal saline and two tablets inserted into the vagina for twelve days. This organism cannot survive at $pH4$. C. M. Wenyon (1920) has examined sections ...

causes ... doubtful whether all these trichomonads are in fact distinct entities, because he has been able to establish *T. intestinalis* in the monkey vagina.

Whittingham goes so far as to correlate neurasthenia with intestinal *infection with flagellates. He sustains his hypothesis by pointing out* that there is a chronic and unremitting irritation of the intestinal ... *ending eventually in neurasthenia* ... and irritability, ... Neurasthenia, ... intestinal flagellates, being also observed with amœbic dysentery and other forms of *bowel disease*

Many observers, including H. M. Woodcock (1917), have seen *Trichomonas* ingesting red blood-corpuscles, but this is, possibly, not a normal happening. Others, for example, K. Tsuchiya (1925), in a detailed study of twenty cases heavily infected with *Trichomonas*, *conclude that the organism is a harmless inhabitant of the* large intestine, and that, whether numerous or scanty, it does not cause disease. On the other hand, W. E. Musgrave (1922) believed that *Chilomastix* may cause diarrhœa

Summary.—The author believes that the presence of *Trichomonas*, *Embadomonas*, *Chilomastix*, and other flagellates in the human bowel in

B M. Das Gupta has shown that the cysts, when scanty, can b demonstrated by the Willis flotation technique employed for ar tome ova

In F. Noc's case (1920) *Isospora* was associated with cysts of *G* in E. Reichenow's (1925) with cysts of *E. histolytica*, ancylostom and a coincident infection with subtertian malaria, and in th described by Smyly and Kme (1936) with cysts of *E coli* and *E*

H Gaillard (1936) found in Saigon a pure infection of *Isospo* child of two years of age who was suffering from acute diarrhœ the fifth day the patient died, and at autopsy the whole int tract was minutely examined without any lesion being detect number of others have been recorded in Europeans in Indo-Ch R Pons, Dufossé, and A Léger C Coreuff (1936) has report cases from Morocco associated with diarrhœa and Charcot-I crystals C. M Ter-Matevossian and A T Tsaturian (1933) f child of five suffering from diarrhœa of fourteen days' duration Caucasus, and *Isospora* parasites were numerous in the fæces

Two cases of *Isospora* infection, both from South America come under the author's notice during recent years As it ha the invariable practice to make a microscopic examination of th in every case, the small number may be taken as a further ind of the comparative rarity of this infection (Fig 50)



Fig 50.—Cysts of *Isospora hominis* with Charcot-Leyden crystals in the fæces.

strated. The fæces were liquid, brownish-yellow and contained

r pus cells were observed,

The outstanding feature

gested material, especially fat. The oöcysts persisted for thirty-six days, after which they vanished and the patient recovered. Signs and symptoms, which were neither prominent nor severe, consisted of diarrhœa, abdominal discomfort, some flatulence, loss of weight, and a certain degree of lassitude. Treatment consisted in the administration of bismuth salicylate and charcoal three times daily.

Ætiology.—*Isospora hominis* (Railliet and Lucet, 1901), also known as *Isospora belli* (Wenyon, 1923), is probably a parasite of the epithelial cells of the small intestine, and it is likely that in this situation the full development will eventually be discovered. The oöcysts vary in length from 25–33 μ and are almost half as wide as they are long. When found in the freshly passed human fæces they are transparent and colourless. An account from the zoological aspects is given in the Appendix (p. 548).

The most exhaustive and detailed account of the infection is by

Iraq	20	Portuguese East Africa	1
Eastern Mediterranean	33	South Africa	1
Italy	2	Senegal	1
Syria	2	North China	3
Turkey	1	Wuchang (China)	1
North Africa	1	Bengal	4
Persia	3	Indo-China	6
Southern Russia	5	Philippine Islands	2
Uruguay	1	Dutch East Indies	6
Argentine	3	Hawaii	1
Brazil	8	U.S.A.	13

Leyden crystals.

diarrhœa may lead to cramps, pinched features, washerwoman's fingers, suppression of urine, and collapse Such attacks are deceptive and may readily lead to a mistaken diagnosis Where there is any reasonable doubt a thick-film and thin-film blood examination for malaria parasites should be performed as a routine, when trophozoites of *P. falciparum* are usually revealed

Very often the spleen may be enlarged, but this is by no means invariable. Although the nose and extremities may be algid and the temperature subnormal, axillary and rectal temperatures will be found raised

Sometimes dysenteric symptoms are present, with the passage of blood and mucus They may be accompanied by hæmatemesis or hæmorrhage from the bowel, and in these cases it is difficult to decide whether the dysenteric syndrome is brought about solely by malaria or whether there is also an associated infection with bacillary dysentery In fact, in malaria cases terminal infections of bacillary and amœbic dysentery were occasionally encountered during the 1914-18 War. This was also noted by L Dudgeon and C Clarke in Salonica, while D. Graham (1918) frequently isolated dysentery bacilli from malaria cases with dysenteric symptoms.

Pathology.—Bignami first described punctate hæmorrhages in the mucosa. The vessels of the stomach wall and the large and small

following changes have been described (*a*) intense infection of the mucosal vessels with parasitized cells, (*b*) necrosis of the epithelium, (*c*) leucocytic infiltration of the tissues subjacent to the necrotic zones, and (*d*) invasion of the necrosed tissues with bacteria.

In his series of cases C. F. Craig described similar changes and even ulceration of the mucosa The intestinal canal was found to contain blood-stained mucus shortly after death

cotton-wool or are scraped, a congested and superficially ulcerated area is left Arafa made preparations from the ulcerated surface, which show large numbers of degenerated endothelial cells and red blood-corpuscles, and on one occasion he was able to confirm the diagnosis by finding a subtertian malaria gametocyte (crescent) in the exudate

Further evidence of the correctness of the diagnosis can be obtained

The case of a commercial traveller was investigated in December, 1933. He had been touring round the West Indies, Bahamas, and British Guiana, and had become infected with *Isospora*. There was little doubt that the symptoms were definitely due to this infection. *The syndrome was singularly* similar to that described by Connal. The patient had suffered from chronic

further three days, after which they disappeared. An opportunity presented itself of re-examining this patient two years later, when the fæces were proved to be normal

The second was that of an explorer who had contracted amœbic dysentery in 1932 on the Amazon, and symptoms had persisted for two years When he was examined the familiar signs and symptoms of intestinal amœbiasis were present, so that it was difficult to assign any pathogenic role to *Isospora*.

years later and the fæces were then quite normal.

it produces are those of a subacute dysentery, with the passage of light-coloured fæces containing much undigested material, an excess of fat, and a number of Charcot-Leyden crystals.

MALARIAL DYSENTERY

Gastro-intestinal disturbances are frequently observed in severe cases of subtertian malaria (*Plasmodium falciparum*). Severe diarrhœa, unaccompanied by fever and often ending fatally, which, in its intensity

The choleraic symptoms may develop unaccompanied by rigor or any of the more familiar signs of subacute malaria, or they may follow on an acute attack. The stools suddenly become profuse, *numerous*
or they may be mucoid with admixture of blood. On
of the sub-
Usually the
but it may
it upon *the*

were observed.

Treatment.—All cases of enteritis occurring in association with subtertian malaria should be treated seriously. It is probably best to commence treatment by intramuscular injections of quinine bihydrochloride (7–10 grains). In more urgent cases it may be necessary to inject the same amount intravenously Thereafter, if the patient is *able to retain it, anti-malaria treatment should be continued with* atebrin, one tablet three times daily after meals for seven consecutive days.

It is sometimes necessary to reinforce the atebrin treatment with small doses of quinine hydrochloride (5–10 grains) taken by the mouth To check the diarrhœa a bismuth-and-magnesia mixture, together with opium, should be employed Should the diarrhœa continue in spite of these measures, gentle lavage of the bowel with normal saline or 2-per-cent sodium bicarbonate, is advisable

LEISHMANIAL DYSENTERY

cases of infantile kala-azar in Sicily, noted the constant presence of entero-colitis associated with circular ulcers in the large intestine The two cases described by H M Perry (1922) merit special consideration

In these the jejunum appeared thickened without any ulceration,

They could be demonstrated in scanty numbers in the submucous coat, and in that position occurred in the endothelial cells,

of escape of viable parasites via the intestinal canal. In dysenteric fæces so often passed by kala-azar patients in the terminal stages of

by observing through the sigmoidoscope the healing of the intestinal lesions following anti-malarial treatment

17 .
di
pc
bloody stools, consisting of gelatinous bright-red mucus resembling those of acute bacillary dysentery. No enlargement of spleen Microscopically, exudate in stools consisted of red blood-cells, intestinal epithelium, and few pus cells Stool plated out for dysentery bacilli, but only *B. coli* and *B. acidi lactici* isolated.

After quiescent interval symptoms recurred with rigor and temperature of 104° F. Numerous subtertian malaria rings in peripheral blood and in stained preparations of the exudate in the stools Quinine (25 grains) given intramuscularly with great improvement

30, x/17
Palestine
no enlarge
Microscopi
Tongue dirty, icteric facies Blood examination showed numerous rings and crescents of subtertian malaria Sudden death four hours after. At autopsy, liver and spleen greatly engorged and tense and of greyish colour; grey discoloration of pancreas Dense injection of intestinal capillaries Rose red

pallor, choleraic diarrhœa with incontinence, sunken, navicular abdomen, no enlargement of spleen Dry tongue, sores on lips, icteric sclerotics, stools incessant, choleraic, offensive Purple discoloration and icy coldness of extremities Blood examination, large numbers of subtertian rings and sporulating forms Death after intravenous injection of 7 grains of quinine.

At autopsy, great enlargement of tense grey liver and spleen, the latter spherical and swollen like miniature football. Great injection of intestinal capillaries Rose-red discoloration and œdema of intestinal mucosa. All vessels choked with sporulating subtertian parasites

The following tragic history emphasizes the necessity of recognizing the gastro-intestinal symptoms as indicative of a severe subtertian malaria infection which may eventually end in coma.—

A man of fine physique who had travelled far in the Middle and Far East for the previous twenty-five years, paid a visit to the Gold Coast for the

serious and he had a rigor A blood film showed an overwhelming infection with subtertian malaria, though the spleen was not palpable. After admission to hospital, he rapidly became unconscious, with cerebral symptoms, and he died in coma, not alleviated by intensive intravenous quinine therapy, on the following day. The cerebro spinal fluid was under considerable pressure All the organs of the body, including the meninges, the brain, spleen, liver, and intestinal walls contained sporulating subtertian parasites, and in peripheral blood films melanophagy and phagocytosis of sporulating parasites were observed

Treatment.—All cases of enteritis occurring in association with subtertian malaria should be treated seriously. It is probably best to commence treatment by intramuscular injections of quinine bihydrochloride (7–10 grains). In more urgent cases it may be necessary to inject the same amount intravenously Thereafter, if the patient is able to retain it, anti-malaria treatment should be continued with atebrin, one tablet three times daily after meals for seven consecutive days

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LEISHMANIAL DYSENTERY

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striking. They could be demonstrated in scanty numbers in the submucous coat, and in that position occurred in the endothelial cells, derived from vascular endothelium They were also present in larger numbers, in the same intracellular situation, in the base of the villi, but in their centres rapid multiplication had taken place (Fig 51)

This peculiar pathology led Perry to speculate upon the possibility of escape of viable parasites via the intestinal canal In dysenteric fæces so often passed by kala-azar patients in the terminal stages of

the disease parasites have been ...
found boc
in whom c
tion of cre
A. Critten
H A. de



Fig. 51.—Microscopic section of the large intestine in kala-azar.
I, Arrangement of the Leishman Donovan bodies in the intestinal cells, II and III, the "bodies" as seen under a higher magnification.

demonstrate these parasites consistently in the stools of kala-azar dysentery with bacillary dysentery characters There was much blood and mucus, and films showed *Leishmania* in the exudate on two successive days.

In the artificially-infected hamster, H E Meleney has found similar changes in the gastro-intestinal tract, the submucosa being filled by

it occurs under natural conditions Shortt, Smith, and Swaminath succeeded in producing infection in one hamster which had been fed during a period of 467 days and on 160 occasions with fæces from kala-azar patients

The Helminthic Dysenteries

CHAPTER XVII

BILHARZIAL DYSENTERY, ŒSOPHAGOSTOMIASIS, HETEROPHYIASIS, FASCIOLOPSIASIS, AND STRONGYLOIDIASIS

BILHARZIAL DYSENTERY

Synonym.—Schistosomiasis

Definition.—This is a group of diseases caused by three species of flukes or trematodes, belonging to the genus *Bilharzia*,* which live in the venous system of man There they produce large numbers of eggs which are extruded through various organs of the body, especially the bladder and bowel Considerable damage is caused to the mucous membrane, and there are pathological changes in the liver and other organs due to toxins excreted by the parasites and to irritation caused by eggs

It is not proposed here to consider the minutiæ concerning this

Ætiology—The parasites are digenetic trematodes, varying in length from 9 mm (*B. japonica*) to 2 cm (*B hæmatobia*) They are unisexual, the male being the stouter and shorter The female is enclosed in a groove caused by ventral infolding of the sides of the body of the male, this groove being termed the gynæcophoric canal Both sexes are provided with an oral and a ventral sucker The

canal consists of an œsophagus which bifurcates form[illegible] two main

male consists of four to nine testes and a corresponding number of

* Cobbold named the genus *Bilharzia*, after its original discoverer, in 1854, and this name therefore, has priority over *Schistosoma*

vasa efferentia opening into a seminal vesicle, the number varying in the different species. The reproductive system of the female consists of an oval elongated ovary, from the posterior end of which arises the oviduct which on passing forward is joined by the vitelline duct; the yolk glands, or vitellaria, occupy the posterior part of the body. The shell-gland opens into the oviduct, which then becomes the uterus, and the genital opening is situated medially just posterior to the ventral sucker.

The *eggs* vary in shape and structure in the three species (Figs. 52, 53),



Fig. 52.—*Bilharzia hæmatobia* eggs in smear made direct from rectum. (× 130.)

(*Photomicrograph, Dr H K Griffin, Amer. Miss Hosp, Assiut, Egypt*)

and measure in length from 60μ (*B. japonica*) to 150μ (*B. hæmatobia*), averaging 60μ in breadth. The egg is provided with a spine, which in *B. mansoni* is placed laterally and in *B. hæmatobia* terminally; in *B. japonica* there is a rudimentary lateral spine in the form of a minute papilla or excrescence.

Geographical distribution.—*B. mansoni* is distributed throughout the continent of Africa, being most abundant in Egypt, the Congo, French West Africa, and Nigeria. It is also common in South America—in Brazil, Venezuela and Dutch Guiana—and in the Antilles, especially Antigua. In some of the West Indian Islands the local feral monkeys

the South African War, infection was imported into Perth, Western Australia, but has since died out. *B japonica* occurs most commonly in China, where its main habitat is the Yangtse valley. It is also found in southern Japan, Upper Burma and southern Philippines Wherever it occurs, it is a natural infection in cats, pigs, dogs and cattle, which act as reservoirs of the infection to man It can easily be transmitted to monkeys, rabbits, and other laboratory animals

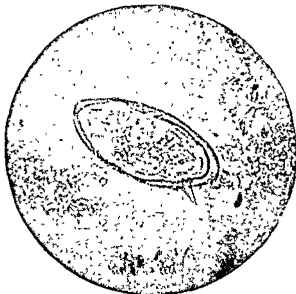


Fig 53 —Lateral-spined egg of *Bilharzia mansoni* in the fæces (× 250.)
(*Microphotograph, Dr. Kerr*)

Life history —The life history of these three parasites is in the main similar Both sexes live in the venous system. The majority of *B mansoni* and *B japonica* are found in the portal and mesenteric veins, and in the vicinity of the liver, but most *B hæmatobia* are found in the lower mesenteric bran he of the ... esico-prostatic and

... Occasionally they

... ins.

The number of eggs laid by the different species varies In *B mansoni* usually only one or two are found in the uterus, the greatest number

... nt, and

... species

... means

of the prehensile suckers enters veins, as her small size enables her to do. There she ejects an ovum from the genital opening situated just posterior to the ventral sucker. Usually the blunt, conical end *of the egg is directed against the venous flow, while the posterior*, bearing the spine, points in the direction of the blood current. The bilharzia then withdraws, and the venule contracts down upon the egg, *holding* it in position Another egg is *deposited* as she withdraws further, and so on. Finally, when all the eggs have been deposited, the outline of the venule resembles a string of sausages (P. H Manson-Bahr and N H. Fairley, 1920).

When the female has withdrawn, the blood current, flowing through the venule containing eggs, forces the eggs through the coats of the vessel so that they gain the lumen of the bladder or intestine Escape

occasionally in the lung but quite commonly in the brain. The bladder is unaffected

in a gyrating fashion, propelled by its cilia, for a maximum of twenty-four hours, after which it expires The miracidium is provided with an anterior papilla or proboscis from which may be traced two salivary

some

-water

these

three, in which alone they can continue development. Boring through the antennæ of the mollusc, the miracidium makes its way into the liver or digestive glands and becomes a *sporocyst*, in the interior of

differences in size and structure between the cercariæ of the three

to swim

is in inner

his skin,

or blood-

vessels, the immature flukes (*schistosomula*) proceed to the liver and the region of the portal vein, where in about six weeks they become differentiated into male and female bilharzia which soon produce characteristic eggs According to the work of Japanese observers, the cercariæ derived from one particular snail develop into flukes of one sex, there are therefore male- and female-producing cercariæ When once the flukes have attained maturity, it is probable that they can live many years, sometimes as many as thirty, their longevity being quite disproportionate to their size

Freshwater snails or intermediate hosts —The following species have been found to harbour bilharzia.—

INTERMEDIARY HOSTS FOR B MANSONI —

Egypt	*Planorbis boissyi*
Tunis	*P philippici sub-angulatus*
Sudan	*P sudanicus*
Nyasaland	*P neo-sudanicus*, possibly *Melanoides tuberculata* (W. L Gopsill)
Zanzibar	*P gibbonsi*
South Africa	*P pfeifferi*
Natal	*Physopsis africana*
Brazil	*Planorbis olivaceous*
Dutch Guiana	*P olivaceous*
Central Brazil	*P centimetralis*
North Brazil and Venezuela	*P guadeloupensis*
	P glabiatus
Antigua	*P. guadeloupensis*
	P antiguensis

INTERMEDIARY HOSTS FOR B HÆMATOBIA :—

Egypt	*Bulinus contortus*
	B dybowski
	B. innesi
	B. forskali
Palestine	*B. truncatus*
Sierra Leone	*Physopsis globosa*
Natal	*Physopsis africana*
South Africa	*Planorbis pfeifferi*
Portugal	*Planorbis corneus*, var. *Metijensis*
Nyasaland	*Melania nodocincta* (Natal, rarely)
	Limnæa natalensis

INTERMEDIARY HOSTS FOR B JAPONICA :—

South Japan and Central China	*Oncomelania nosophora* (Robson, 1915)
China	*Oncomelania hupensis*
Philippines	*Blanfordia quadrasi*
Formosa	*Oncomelania formosana*
Japan (Island of Sadi)	*Blanfordia japonica*

It is not proposed to give a minute description of the above molluscs. The snails of the genus *Planorbis* are flat, Ammon-horn-shaped snails which float on the surface of the water, those of the genus *Bulinus*

and *Physopsis* are squat, spiral snails with an apical whorl and a

[illegible]

form of pipe-stem cirrhosis is eventually produced. The passage of the eggs into the intestinal canal gives rise to a series of peculiar changes. The mechanism has already been described, and the number of eggs in these tissues, especially in colon and small intestine, may be enormous. Dysenteric symptoms are produced in six to fourteen weeks from the



P. H. M.-B.

Fig. 54.—Microscopic section of the large intestine in intestinal bilharziasis, showing eggs of *B. mansoni* and *B. hæmatobia* in situ.

time of infection, while focal lesions—polypi and adeno-papillomata—are formed in from eight to fourteen weeks. (Fig. 54.)

N. H. Fairley (1920) has studied the minute changes in the tissues in artificially-infected monkeys, and has found that in these animals the earlier pathological changes are due rather to toxins than to mechanical irritation, and that a *characteristic* cellular humoral response is evoked. In monkeys death ensues from the second to the sixth week, usually associated with intense melæna. The earliest localized lesions very *closely resemble those of tuberculosis and are*

known as pseudo-tubercles. They are small whitish nodules, varying in size from 0 5 to 4 mm in diameter, and consisting of fibroblastic cells with large numbers of eosinophils Originally described in monkeys, they have now been confirmed in man by P. H J Lampe (1926) in Surinam, notably in the mesenteric glands, where they simulate tuberculous lesions closely In that country 18 18 per cent of autopsies show pathological changes due to this parasite These pseudo-tubercles are scattered throughout all the organs, and especially on the peritoneal coats of the bowel They may also occur on the

lymph-glands and those of the retroperitoneal tissue are usually enlarged The appendix may be affected, giving rise to bilharzial appendicitis There is usually very distinct enlargement of the spleen,

associated with papillomata, (4) polypi of the bowel, which may lead to intussusception, (5) cauliflower excrescences in the neighbourhood of the anus One or all of these conditions may eventually undergo secondary malignant changes

The presence of the eggs in the tissues can best be demonstrated, according to A R Ferguson (1913), by digestion of the material in 3 5 per cent solution of caustic potash at a temperature between 60°

hæmorrhage without visible ulceration When this process has lasted

rule, are more numerous in the vicinity of the rectum Sometimes they occur clustered in definite groups with healthy tracts of mucous membrane intervening; very often adeno-papillomata co-exist with the diffuse deposition of the eggs already described (Fig 55) As these

papillomata enlarge they often become elongated. They may be torn off by the peristaltic action of the intestines, thus causing sloughing, with formation of round clear-cut ulcers When these ulcers are [illegible] especially if they are secondarily infected, acute [illegible] with blood and pus in the stools [illegible] may lead to [illegible]

and ileum are [illegible]
are usually associated with periconitis [illegible].



P H M-B.

Fig. 55.—Intestinal bilharziasis (*B. mansoni*), showing adeno-papillomata in the rectum.

Liver —In early stages of the infection the liver is slightly enlarged and is finely mottled and greyish in appearance. Internally it exhibits numerous minute dull-white nodules, due to a degeneration of the liver cells produced by toxic necrosis. In the centre of these nodules eggs are present, usually singly or in groups, surrounded by a leucocytic zone consisting mostly of eosinophil cells. At a later stage it becomes somewhat reduced in size and the tissue is intersected by delicate fibrous strands, especially in the periportal zones This cirrhosis is not sufficiently marked to produce pressure on bile-ducts or veins, and secondary jaundice is absent. Immature bilharzia worms are found in the portal veins, and eggs are distributed throughout the liver.

The final expression of bilharzia disease is " clay-pipestem " cirrhosis.

The liver may be enlarged, although even in its extreme development this organ may not suffer any great diminution in volume. There is always a certain amount of perihepatitis, but the external surface is not "hob-nailed" or strikingly irregular as in other forms of cirrhosis. The internal cirrhotic changes are more pronounced than would be inferred from inspection of the exterior In all directions prominent [illegible] duct formation takes place

The pathology of *B japonica* infection is similar to that described.

Symptoms.—In the early stages toxic symptoms resembling those of the Katayama disease of *B japonica* are noted, especially in Europeans who have become heavily infected The general signs consist of a high remittent fever with urticaria, marked abdominal pain, loss of appetite, rigors, and pulmonary symptoms This stage, which may last six or eight weeks, was commonly seen in soldiers who became infected in Egypt in the early stages of the 1914-18 War. After the infection has lasted two months or more, symptoms become localized, with passage of dysenteric motions, and there is little in general to differentiate them from mild attacks of amœbic dysentery.

In the terminal stages of the disease, large massive abdominal tumours may form, giving rise to discomfort and intestinal stasis, the liver becomes markedly cirrhotic, and ascites may be present At this stage there is little to distinguish the clinical picture from that of other forms of ascites, indeed, hæmatemesis from rupture of distended œsophageal veins may take place

Infiltration of the buttocks with eggs which have penetrated the [illegible] vene and may often be choleraic in character These are the major manifestations of severe bilharzial disease On the other hand, slight infections are extremely frequent and probably make up the greatest number of cases diagnosed The eggs are then discovered accidentally in the laboratory while the fæces are being examined They may be present in persons who have been exposed to infection on one or two occasions and whose general health remains good It is most necessary, however, that *all* cases should be treated, because ultimately the disaster of cirrhosis of the liver is likely to take place Symptomless cases are a danger, also, as carriers of the disease.

A totally different clinical picture may be presented in visceral

papillomata enlarge they often become elongated. They may be torn off by the peristaltic action of the intestines, thus causing sloughing, with formation of round clear-cut ulcers. When these ulcers are numerous, and especially if they are secondarily infected, acute [illegible] the glands

[illegible]

and ileum are extremely rare. The adeno-papillomata of the [illegible] are usually associated with pericolonic nodules.



Fig. 55.—**Intestinal bilharziasis (*B. mansoni*), showing adeno-papillomata in the rectum.**

Liver.—In early stages of the infection the liver is slightly enlarged and is finely mottled and greyish in appearance. Internally it exhibits [illegible] to dull-white nodules due to a degeneration of the [illegible]

[illegible]

zone [illegible] becomes somewhat reduced in size and the tissue is [illegible], delicate fibrous strands, especially in the periportal zones. This cirrhosis is not sufficiently marked to produce pressure on bile-ducts or veins, and secondary jaundice is absent. Immature bilharzia worms are found in the portal veins, and eggs are distributed throughout the liver.

The final expression of bilharzia disease is "clay-pipestem" cirrhosis.

cytes may be present; later, progressive microcytic anæmia becomes apparent and finally there is a leucopenia of about 3,000. There is usually a considerable increase in the eosinophil cells The differential diagnosis from splenic anæmia is not always easy; in the latter there is usually a leucopenia with increase of lymphocytes, absence of eosinophils, and increase of blood-platelets

A parallel and similar splenomegaly occurs in *B japonica* infections and is known locally as "Katayama disease"

Diagnosis.—The diagnosis of *B mansoni* and *B japonica* infection is made by the discovery of the characteristic eggs in the fæces under a microscope with low power Usually they are very scanty, and it is necessary to examine several fæcal films before arriving at a negative diagnosis A concentration method which is very successful has been described by F. Fulleborn A small quantity of fæces, the size of a hazel nut, is placed in a conical glass, carefully rubbed up with a glass rod in a few cubic centimetres of 2½-per-cent salt solution, and put away to settle in the dark for five minutes The solution is poured off the sediment and this process is repeated two or three times The *Bilharzia* eggs remain in the sediment, which is then mixed with distilled water at 120° F and exposed to a bright light The miracidia immediately escape from the eggs and can easily be seen with a hand lens, particularly against a dark background By adding a few drops of perchloride of mercury solution the miracidia are killed and can be found and recognized in the sediment

Two other aids to diagnosis may be mentioned the intradermal test of Fairley, which is performed with an antigen made from the cercariæ in the snail's liver, and the complement-deviation reaction of the same worker This is useful also in *B hæmatobia* and *B japonica* infections, and is positive in about 85 per cent of the cases Sometimes, when the blood serum is negative to this test in the advanced stages of the disease, ascitic fluid gives a positive reaction

In cases of localized rectal disease, and especially where the masses resemble thrombosed piles, if *B mansoni* or *B japonica* be suspected, the [illegible] orceps, crushed [illegible] oscope for eggs.

A G Biggam [illegible] early stages small patches of granulation tissue can be observed at the bifurcation of blood-vessels in the mucosa In these hyperæmic areas typical small, round, deep red spots, which are very characteristic of early bilharzial affections, are seen dotted about on the surface of the mucosa N H Fairley (1933) has also noticed small pale elevated tubercles, much resembling the "pseudotubercles" found in experimental bilharziasis in artificially-infected monkeys Later, polypi, localized thickening of the large intestine, and adeno-papillomata may be recognized Fæces may be removed from the rectum with the biopsy forceps and examined

infection known as *Egyptian splenomegaly*, a syndrome in which, some authorities hold, infection is by one sex of the worm only. This is a common disease in Egypt and Northern Nyasaland, possessing many features resembling kala-azar. Anæmia, febrile disturbances, cirrhosis of the liver and ascites are the main features. It is endemic in Egypt, the Sudan, and Nyasaland, where 20 per cent. of children under four years of age are found to be sufferers in various degrees. The hyperplasia of the spleen is, to a great extent, secondary to the hepatic cirrhosis, intestinal symptoms are usually absent and eggs of the parasite cannot be found in the stools. The fever is generally irregular, of an intermittent type. The enlargement of the spleen



Fig. 56.—Rectal papillomata produced by eggs of ***Bilharzia hæmatobia.***
(Dr H K Griffin, Amer. Miss Hosp., Assiut, Egypt)

causes pain and discomfort, especially after meals, and gives rise to a *dragging sensation on exertion.* The final stages are ushered in by cirrhotic changes in the liver, which becomes progressively harder, and finally shrinks within the costal margin. The spleen also becomes fibrotic, but does not proportionately decrease in size. Finally, the patient dies with symptoms of hepatic cirrhosis, ascites, and emaciation. Quite commonly, thrombosis of the portal vein takes place. Splenectomy, performed before the onset of ascites, has been successful; H E. S *Stiven (1928)* has reported upon 390 cases, with a mortality rate of 13 per cent

The blood-picture *varies in different stages of the disease.* In the early stages there is a distinct leucocytosis of about 17,000, and myelo-

dysentery, but the author has shown that eosinophil leucocytes are usually present in preponderating numbers When pericolonic masses are found in association with enlarged mesenteric glands, especially in children, the differential diagnosis from abdominal tuberculosis may be difficult

Treatment.—*B mansoni*, *B japonica* and *B. hæmatobia* infections are treated by intravenous injections of antimony, thus killing the adult worms The gross changes in the organs of the body are more severe in the two former infections, because of toxic absorption Intravenous injections of tartar emetic are given on alternate days, commencing with

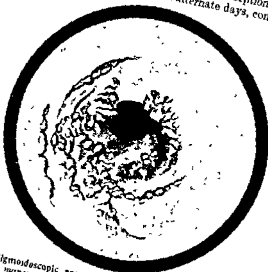


Fig. 58 —Sigmoidoscopic appearance of a case of bilharzial dysentery (*B mansoni*), showing characteristic adeno-papillomata. (*After A G Biggam*)

half a gram of tartar emetic (sodium antimony tartrate) dissolved in 10 c c of freshly-distilled, sterile water This amount is gradually increased, half a gram at a time, until the maximum individual dosage of 2 or 2½ grains is reached Some authorities are in favour of dissolving the drug in a 5 per cent glucose solution as this neutralizes, to some extent, the toxic effects of the antimony

In Egypt, since 1925, the course consists of twelve injections three times weekly until 22½ grains have been injected, this usually occupying about four weeks When a small amount of diluting fluid is used, as suggested above, very few of the toxic symptoms due to antimony—such as headache, cough, nausea, and transient

under the microscope for eggs. Portions of papillomata, when teased out in saline and examined, may also reveal ova. (Fig. 57.)

The papillomata may be either sessile or pedunculated, and may be so massive as to obstruct the lumen of the bowel (Fig. 58) Their colour is usually redder than that of the surrounding mucosa, and sometimes actual hæmorrhages are seen. Seldom do lesions resemble the punched-out depressed ulcerations of amœbiasis, though sometimes both infections are associated. Treatment with intravenous injections of emetine and tartar emetic exerts no curative effect upon fully-developed papillomata



Fig. 57.—Lateral-spined egg of *B mansoni* in specimen obtained by sigmoidoscopy. Note that the shape of egg and size of spine differ materially from similar specimens seen in the fæces.

re…

pe…

transverse and pelvic colon

Differential diagnosis is the same as for other forms of dysentery, especially the amœbic form As in other tropical diseases, a very confusing situation occurs when more than one infection is present. In natives of Egypt a terminal infection with amœbic or bacillary … necessary … correct … amœbic

conclus…

veins are too narrow for intravenous injections The initial dose is

mucous tube may be loosened by the gloved finger and withdrawn until the upper limit of the papillomata is reached Lengths of from 12–15 inches of the mucous membrane can be removed in this way The

Surgical treatment of the pericolonic tumours in the abdomen

always associated with cirrhosis of the liver, and call for persistent tapping and withdrawal of ascitic fluid at frequent intervals—a wearisome process. Omentopexy has been tried but has not been very successful Splenectomy has been undertaken by Owen Richards, Coleman and Bateman with considerable success The latest reports show that a preliminary treatment for five or six weeks is necessary This consists of a course of twelve tartar-emetic injections, together with carbon tetrachloride in those cases which are infected with ancylostomes, and with a full course of neosalvarsan in those complicated by syphilis Immediately before the operation the patient should be given a rhubarb-and-soda mixture for one week, and then iron and arsenic to restore the blood Stiven advocates, in addition, an injection of pneumococcic vaccine on the eve of the operation, to guard against pneumonia Under the most favourable

rheumatic pains—have been noticed. P. H. J Lampe, in Surinam (1926), has worked out a system for treating out-patients with three injections of a 1 per cent. solution of tartar emetic (3 c c , 5 c c., and 7 c.c) during each week. A total of 25 to 30 grams is administered, the course occupying six or seven weeks. A rectal injection of tartar emetic for young adults and children in whom, for some reason or another, the intravenous route cannot be employed, has been worked

necessary. Khalil has described a number of cases of bilharzial infection which appear to be antimony-fast, and he suggests that they are due to too rapid excretion in the urine.

The pentavalent preparations of antimony, by the intravenous route, have not proved to be as efficient as in kala-azar and other leishmania infections. Recently fouadin (Bayer) has been used in Egypt by

Nine to twelve injections of a 7 per cent. solution given by the intramuscular route are said to be sufficient to cure the majority of cases The following scheme has been advocated :—

1st day	1 5 c.c.	11th day	5 c c.
2nd day	3.5 c c.	13th day	5 c.c.
3rd day	5 c c	15th day	5 c.c.
5th day	5 c c	17th day	5 c c.
7th day . . .	*5 c.c.*	*19th day*	5 c.c
9th day . .	5 c.c.	21st day	5 c c.

The drug causes little or no reaction, and abscess formation and ... At

en

of

though not necessarily serious, symptoms.

is the experimental

worms. This was,

of the antimony-

intramuscularly to

children who are intolerant of antimony tartrate, or to those whose

Amazon. Autopsy in the latter case showed that the patient died of septic peritonitis due to the lesions caused by this worm.

A man of thirty-six years was admitted to hospital suffering from acute dysentery; he became delirious and died within three days

A metre of the surface of the small intestine, extending from the ileo-cæcal valve, was studded with small, raised, dark-coloured tumours, the majority of which were found in the lower part of the ileum within 35 cm of the ileo-cæcal valve. The nodules were less numerous and pronounced in the remaining 65 cm of the infected bowel Most of the growths were small and oval, they varied in size from that of a small pin's head to [illegible]

found penetrating the mesentery

[illegible]

of the horse

R T Leiper has emphasized the fact that the nodules on the peritoneum look very like those of tuberculosis, and, being described as such, are often missed It may be, therefore, that œsophagostomiasis is a more common infection than has been supposed.

Ætiology.—The species which was found by Thomas and described as *Œsophagostomum stephanostomum* (var *Thomasi*), differs only in minor details from the commoner species, *Œsophagostomum apiostomum* [illegible]

The copulator [illegible]

breadth, which are passed in an advanced stage of development, closely [illegible]

Treatment.—There are reasons for believing that phenothiazine, by mouth in tablet form (2–4 grm), is lethal to the œsophagostome The course is continued for 5–7 days On account of its toxic properties this drug is unsuitable for children

conditions the minimum mortality is about 13 per cent. The average weight of the spleens removed by the aforementioned surgeons is 3¾ lb. The favourable effects appear to be permanent and ascites does not develop later.

This then ... [illegible]

Congo, may not be involved.

Another species of Bilharzia has been found in man in Southern Rhodesia by W. K. Blackie. This is known as *B. mattheei*, normally a parasite of sheep and cattle, and has been demonstrated in the genito-urinary tract and, in one instance, in the bowel. The eggs are much longer and more pointed than those of *B. hæmatobia*, and measure on an average 210–240μ by 40–70μ.

Little need be said about the treatment of the dysenteric symptoms produced by *B. japonica*. A larger amount of tartaric emetic is apparently necessary to overcome this infection. According to Faust and Meleney, 22–30 grains of intravenous tartar emetic over a period of 18–20 days are usually curative; but if the patient applies for treatment, as he so often does, when he is in the advanced stages of the disease, when hepatic cirrhosis is well-marked, then such treatment will have little effect.

ŒSOPHAGOSTOMIASIS

Œsophagostomiasis is a dysenteriform condition produced by a small nematode—an œsophagostome—of which there are several species. The larvæ of this worm become encysted in the coats of the bowel, usually in the large intestine, and gradually develop into immature œsophagostomes. They then rupture their cyst-walls and pass into the lumen of the intestine or into the peritoneal canal, where they become adult The mammilated appearance of the mucosa closely resembles that produced by polyposis in man

Anthropoid apes, especially the ourang-outang, certain species of monkey, and some of the domestic animals can be infected by œsophagostomes Weinberg has given a very complete report of the macroscopical and microscopical appearances of the disease in anthropoid apes and monkeys It is a very rare disease in man Brumpt reported the first case in 1905, in a negro from the Omo River, near Lake Rudolph in East Africa, and Thomas the second, from the

Treatment.—Beta-naphthol, two treatments of 30 grains (2 grammes) each, and carbon tetrachloride (3 c.c. for an adult), are specific for this infection

[illegible]

occur in the fæces, and give rise to dysenteric symptoms consisting of dull abdominal pains and occasionally diarrhœa The differentiation from chronic appendicitis may sometimes be difficult

STRONGYLOIDIASIS

Strongyloides stercoralis (Bavay, 1876) is a small nematode which [illegible]

less, transparent, filiform worms measuring 2 2 mm in length by 30–75μ in diameter They bore their way deeply into the epithelium of Lieberkuhn's glands where they deposit their eggs. The male is scarce and is shorter and broader than the female It remains a lumen parasite, having lost its ability to penetrate tissue

The embryos, hatching from the eggs, appear in the fæces as rhabditiform larvæ, usually known as *Anguillula stercoralis* A heterogenic development then takes place in soil, and within thirty hours the larvæ have become sexually mature males and females—free-living, unisexual adults The females produce their eggs from which hatch infective filariform larvæ It has been shown by Fülleborn that these parasites enter the skin and utilize the same route of invasion and migration through the human host as does the ancylostome

Pathogenesis and symptoms.—Ever since A Normand, in 1877, discovered this species of nematode in the fæces in Cochin diarrhœa (sprue), it has been considered to be the cause of intestinal catarrh and diarrhœa. On entering the skin the infective larvæ may produce a localized dermatitis When the intestinal mucosa is invaded a subacute catarrhal inflammation may be produced, giving rise to a diarrhœa with mucus and, it is said, the occasional appearance of occult blood

There is considerable divergence of opinion as to the exact pathogenicity of this parasite In the author's opinion it is quite harmless

Treatment.—[illegible]

[illegible] per kilo body-weight, or, for the average adult male, 1 gr three times daily for 7–10 days

HETEROPHYIASIS

This is a small pyriform fluke found as a natural infection in the cat, dog, fox, and man. It is comparatively common in Egypt and the Far East, including Japan and Formosa.

The worm is very small, measuring only 1–1.7 mm. in length by 0.3–0.4 mm. in breadth, and it lives attached to the mucosa of the small intestine of the human host. The eggs are operculate, oval, and light brown, measuring 28–30μ by 15–17μ. The miracidium, which escapes from the egg in water, develops in fresh-water snails—*Melanoides tuberculata* and *Cleopatra bulimnoides*. The cercaria is an oculate lophocercous larva, sometimes termed *Cercaria pleurolophocerca* (Sonsino), which, on escaping from the snail, attacks the mullet (*Mugil cephalus*) or the minnow (*Gambusia affinis*). M. Khalil has recently traced out the development in quite a different snail, *Pirenella conica*, in Lake Manzala, Egypt. Infection of man takes place through consuming the raw flesh of the fish.

Pathogenesis.—It has been reported by various observers that the presence of these small flukes in the intestine causes a catarrhal state of the bowel and consequent diarrhœa. G Carmichael Low has cited one dysenteric case in which 500 adult trematodes were found in the fæces after the administration of eucalyptus, castor oil, and chloroform mixture.

FASCIOLOPSIASIS

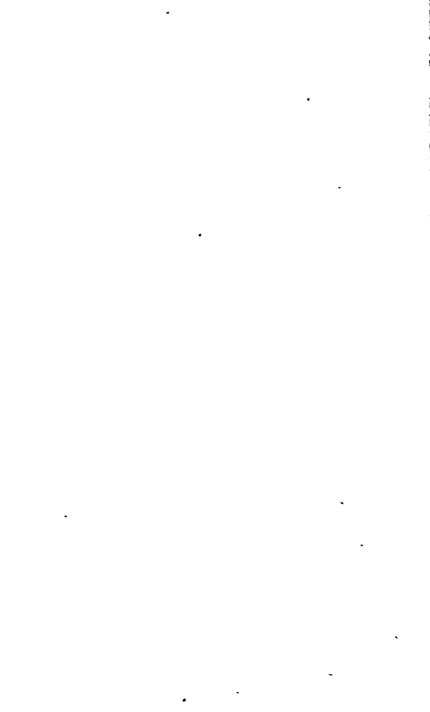
The term fasciolopsiasis denotes intestinal infection by the large leaf-like trematode, *Fasciolopsis buskii*, an Asiatic species and the largest trematode which is parasitic in man. The average length is 30 mm., breadth 12 mm., and thickness 2 mm.

The evolution of this parasite and that of *F. hepatica* are in the main similar. The egg lies in water for two or three weeks, and from it hatches a miracidium which enters and develops in the body of certain species of *Planorbis* snail. The cercariæ, escaping from the snail, encyst on the water-calthrop and water-chestnut which are freely eaten by the Chinese, forming a food known as *ling*.

Pathogenesis and symptoms.—When a few *F. buskii* inhabit the upper part of the small intestine they cause no inconvenience; but when many are present they cause diarrhœa with the passage of offensive stools. The first clinical signs come on about three months after exposure to infection. Grave symptoms, simulating gastric ulcer, indicate the presence of large numbers of parasites. Œdema may be noted, involving the face, abdominal wall, and lower extremities; ascites is common. In the terminal stages the skin becomes rough and dry and diarrhœa is continuous.

Diagnosis.—Diagnosis is based upon finding the characteristic eggs in the fæces. The stools are greenish-yellow and contain much undigested material.

The Infective Diarrhœas



CHAPTER XVIII

PARATYPHOID, TYPHOID AND FOOD-POISONING

Definition.—The term "food-poisoning" should be restricted to acute gastro-enteritis due to bacterial infection of food and drink As employed here, it does not include "botulism," a disease which presents no symptoms of gastro-enteritis

The number of organisms recognized as capable of giving rise to food-poisoning has greatly increased since the isolation of *B. enteritidis* by Gaertner in 1888, and it is now estimated that at least twenty-seven members of the Salmonella group have been identified with actual

[illegible]

before ingestion—or the toxin type.

In the *infection* group of food-poisoning, after a short inoculation period varying from a few hours up to three days, but usually within twenty-four hours, the illness commences with headache, nausea, diarrhœa, and abdominal pains. There is, as a rule, a considerable degree of pyrexia and the temperature may rise to 102° F In cases running a favourable course the symptoms gradually abate so that the patient recovers within a week; but in very severe cases there is restlessness, which is followed usually by cramps, coma, and death At autopsy the mucosa of stomach and intestines is found to be swollen and congested , Peyer's patches are not involved, though minute ulcers may be seen There is usually fatty degeneration of the liver, and the causative organisms can be recovered from the blood, spleen, and other viscera In the type of food-poisoning caused by *toxins*, the general symptoms resemble those of the infection type, but the incubation period tends to be shorter—it may be half an hour to four hours—and vomiting more violent , prostration is greater, but there is less fever so that recovery is more rapid Fatal

SALMONELLA GROUP :—

(a) [illegible]
(b) [illegible]
(c) [illegible]
(d) [illegible]

,, *choleræ-suis.*
,, *ærtrycke* } identical
,, *typhi-murium* } —*B typhi-murium*

OTHER ORGANISMS —

Bacterium sonnei—*B dysenteriæ* Sonne
Proteus vulgaris

The *paratyphoid organisms* may be important, especially in time of war. The Salmonella group is sometimes referred to as the "food-poisoning group," but *B paratyphosus* B is not generally considered to cause outbreaks of acute gastro-enteritis, while the clinical signs and symptoms to which it gives rise are practically identical with those of *B paratyphosus* A

Some authorities place *B typhosus* as well as the paratyphoid organisms among the food-poisoning agencies, but the enteric group (*typhosus*, *paratyphosus* A and *paratyphosus* B) differs from the true food-poisoning group in that the incubation period is longer The enteric group are not natural pathogens of animals such as mice and rats, and their transmission is confined ultimately to human carriers The symptomatology, also, is somewhat different The type of illness caused by the paratyphoid organisms is usually a septicæmia, very similar to that of typhoid, but ulcerations produced are not confined to the small intestine, as in *typhosus*, but may cause lesions of considerable extent in the colon Thus with paratyphoid infections due to paratyphoid B, the initial symptoms were frequently dysenteric in nature, subsequently typical paratyphoid pyrexia ensued

Of course it is possible, as the author has been able to demonstrate, for a double infection of *B paratyphosus* and *B shigæ* to be present, but there have been many cases in which the former was present in pure culture, and in which the pathological appearance of the extensive ulcers in the large intestine sufficed to account for the dysenteric symptoms

Symptoms of food-poisoning.—The symptoms commence almost simultaneously among a number of food consumers, in large outbreaks every degree of severity of illness is present The excreta of those suffering from the poison are infective and thus it is spread to others There is usually an incubation period of three to thirty hours. The

(*B. aertrycke*), given suitable conditions, may produce substances causing gastro-intestinal irritation, and there is evidence that members of the Salmonella group contain thermostable toxic substances which are soluble in water and are precipitated by alcohol. The method of

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organisms, not in themselves strictly pathogenic, such as *B. coli*, *Proteus vulgaris* and *P.*

and out of forty-six in 1935 it was isolated twenty-nine times. In 1937 evidence that *B. proteus vulgaris* can cause mild outbreaks of gastro-

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Usually the meat has been made into pâtés, pies, jellies, or sausages, processes which may involve imperfect cooking and liability to contamination. Usually the food has been recooked, and sometimes it has been prepared and allowed to stand before being eaten. It must be remembered that, as a rule, the food appears quite normal to inspection.

During recent years attention has been directed towards poisoning by eggs, duck eg

their formation in

infection with var

poisoning group

to contaminated cockles

The opportunities for contamination of sound meat during the course of preparation for food are numerous, though it is often difficult to determine the exact manner. The main sources are rats, mice and

CHAPTER XIX

CHOLERA

Synonym : Cholera Asiatica

Definition.—An acute, infectious, epidemic disease caused by Koch's cholera vibrio. It is characterized by sudden onset, purging and vomiting of colourless, watery material, muscular cramp, collapse, suppression of urine, and, very often, sudden death. The mortality is usually very high

History and geographical distribution.—Cholera is endemic [illegible]

travelling eastward as far as Japan, southward to Mauritius, and westward to Syria and the shores of the Caspian Sea. Reaching Astrakhan in 1825, it spread no further. In 1830 cholera first visited Europe, and since that date there have been at least five epidemics—1848–51, 1851–5, 1870–3, 1884–6, and 1892–5 It is true that there have been minor outbreaks since that time, but they have remained very restricted in area In the Balkan War of 1913 and in the course of the Great War, 1914–18, there were a number of epidemics in the Balkans and in Iraq, but the disease did not spread as an epidemic beyond the actual seat of war. In the epidemic of 1870–3, Great Britain was practically spared, but the infection [illegible]

Pacific Islands, South Africa, and the West African Coast, have so far escaped

Of all the cholera-disseminating centres in India, Hurdwar appears to be the most important, for this is a great pilgrim centre, the majority

diarrhœa rarely lasts for more than five days. Continuous vomiting denotes serious prognosis. When improvement sets in it progresses rapidly.

The physical signs cannot be held to be very characteristic. The tongue may be remarkably clean, the abdomen is usually tender, but ... There may ... ire apyrexial. ... frequent are ... mass in the fæces are rare.

The sequelæ of food-poisoning are few; they are usually confined to the large intestine, and take the outward form of persistent diarrhœa or obstinate constipation.

The mortality is usually low, varying from 1 to 8 per cent. In the Limerick outbreak described by McWeeney (1909), nine deaths occurred in seventy-three cases, but in a small outbreak due to *B. œrtrycke* in Halle, Germany, six out of seven cases were fatal.

Diagnosis is usually a fairly simple matter, established upon the ...

Treatment.—The first essentials are to provide warmth to counteract the collapse, and fluids by the mouth or intravenously to dilute the toxins. In the early stages large doses of aperients are indicated, of which castor oil (½ ounce) is the most suitable. For collapse, stimulants such as small doses of brandy or injections of strychnine are indicated. The diet should be carefully regulated and for the first twenty-four hours nothing but fluids should be permitted. The best drug treatment for the gastro-intestinal condition is undoubtedly bismuth, e g bismuth salicylate (10–15 grains) three times daily. For the constipation which so frequently follows the ...

* See also (p 78) F H A Clayton and J W. Hunter have shown that under certain circumstances Sonne's bacillus may cause symptoms closely resembling food poisoning.

bear this out It is generally agreed, however, that ingestion of the bacillus is not the only factor necessary in the production of the disease. Probably the state of health and degree of acidity of the gastric juice render some more susceptible to this infection than others

thousand in the former

To illustrate the second type of water transmission, the well known incident of the Broad Street pump may be cited This was the first definitely proven instance of the connexion between the drinking of water and the onset of cholera In 1854 it was noted that cholera was ten times more prevalent

cholera, and died the following day.

D'Herelle has made the interesting suggestion that the amount of bacteriophage produced in the intestinal canal is a factor in the rise and fall of cholera epidemics Those patients in whose stools no bacteriophage is present die of the disease, while those in whom the bacteriophage is abundant rapidly recover. It is claimed that it can also be demonstrated in contaminated well-water

retain infectivity when damp, moisture being essential to the life of the cholera vibrio

of pilgrims travelling there from the Punjab; by this means cholera spreads all over India. The disease is carried to Arabia, again by means of the pilgrim traffic. In 1865 it was carried by sea from Bombay to Arabia and Mecca, and was then widely spread by the returning pilgrims—throughout Egypt, Syria, and the southern European ports, to the East African coast, to the head of the Persian Gulf and up the Euphrates valley

[illegible]

hundreds of thousands of *human beings are collected together* under highly insanitary conditions. Cholera appears never to travel faster than man, but in modern times, owing to the increased speed of locomotion and the increased amount of travel, epidemics advance more rapidly and pursue a more erratic course than they did eighty years ago.

The endemic prevalence in India is *best illustrated by the average* yearly number of deaths in different provinces during the decade 1898–1907. In Bengal and Behar, the average yearly cholera mortality was 207,118, that is, 2 59 per thousand; in Madras there were 56,809

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favourable atmosphere for its development.

In Lower Bengal and Calcutta, however, the relationship is of a different kind. Here cholera is present throughout the year, having a definite maximal incidence in the dry, hot months of March and June when the water supply is most deficient and contaminated, and

[illegible]

of the disease elsewhere.

Cholera is mainly a water-borne disease, and the bacillus enters by the stomach; there have been numerous historic instances to

bear this out It is generally agreed, however, that ingestion of the bacillus is not the only factor necessary in the production of the disease Probably the state of health and degree of acidity of the gastric juice render some more susceptible to this infection than others

of the area affected, disappearing with almost equal suddenness In the

thousand in the former

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water from the Broad Street well, had a bottle of it supplied to her daily She drank some of the water on August 31, 1854, became infected with cholera, and died the following day

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Ætiology.—It has been said, and well said, too, that although you can eat cholera and drink it, yet you cannot catch it, and this dictum is borne out by the well-known immunity, as long as they do not eat or drink in the wards, of nurses and orderlies in cholera hospitals The

that soiled clothes may be a source of infection, but they can only retain infectivity when damp, moisture being essential to the life of the cholera vibrio.

In India, E. D. W. Greig (1913) stored the rice-water stools of ninety-

Patients who have recovered from cholera may continue to excrete the vibrio irregularly for weeks. As a rule 90 per cent. become free *from infection in fourteen days, and 99 per cent. within a month.*

The cholera vibrio.—The cholera vibrio, or comma bacillus, was first discovered by Koch in Egypt in 1883 and confirmed in Calcutta in 1884. His observations have been abundantly confirmed since that date.

When all the morphological appearances and cultural characters are taken together, the result is fairly distinctive, but since certain other vibrios, e g, that of Finkler, behave in much the same manner, a mistake may easily be made One characteristic reaction given by the true cholera vibrio is that known as the cholera-red reaction (due to the presence of indol nitrite in the medium), in which a red colour is obtained by the addition of pure sulphuric acid or other mineral acid to a cholera culture in 1-per cent. peptone solution. The true cholera vibrio may be further recognized by testing it against [illegible]

The virulence of the cholera vibrio can be raised by passage through guinea-pigs Successive culturing in the peritoneal exudate of these animals is alternated with culture media growths, and virulence thereby becomes enhanced A *fixed virus*, the virulence of which cannot further be affected thereby, results and this formed the basis of Haffkine's cholera vaccine

It is only comparatively recently that all doubts that the cholera vibrio is the genuine germ cause of cholera have been dispelled. On many occasions cultures of the cholera vibrio have been swallowed by way of experiment, but in one single instance only has true cholera been reproduced It is thus probable that, for the production of the clinical condition known as cholera, other factors are necessary in addition to the vibrio The disease can only be produced in lower animals by administering cholera cultures after lowering the general resistance - in ground-squirrels by large doses of alkalis

Inagglutinable vibrios known as paracholeras, such as Finkler-Prior and El Tor, resemble the true cholera vibrio closely, and so, also, do organisms [illegible]

contaminated with bacteriophage.

Toxins.—Filtered cultures of the cholera vibrio exert little poisonous action; the virus is apparently liberated by the breaking up of individual organisms, and dead cultures, when administered by the mouth, produce little effect unless the intestinal canal is injured in some way. These poisonous bodies are mostly destroyed at 60° C., but, when ground up and frozen by liquid air, an extract is obtained which is extremely toxic if injected intravenously into laboratory animals

Immunity—Most laboratory animals, especially the rabbit and the guinea-pig, may easily be immunized against the cholera vibrio by repeated intraperitoneal injections of dead cultures, and the serum thus obtained possesses high agglutinating powers—up to 1 . 20,000 In tests for proving that the vibrios isolated from a given stool are those of true cholera, a serum should be employed which gives a titre of 1 . 4,000. This, when injected into non-immune animals, exerts a protective power four or five times as great against the lethal dose of organisms The active bacteriolysis which takes place is known as Pfeiffer's reaction The test is performed as follows.—

A loopful of a young agar culture of the vibrio is added to 1 c.c. of broth

Pathology.—The appearances found after death naturally vary considerably with the severity and duration of the disease If death occurs in the *algid stage* of cholera, the surface of the body appears shrunken and wizened. Rigor mortis occurs early and persists for

some may actually be found to be ruptured The right side of the heart and all the main veins are distended with dark, thick, imperfectly

they may be found in the urine. They occur in large numbers in the stools in the acute stages of the disease, and in the contents of the intestines Evidence of infection is most abundant in the upper part of the small intestine and duodenum, but may with difficulty be found in the large In microscopical sections vibrios may be found

exhibit symptoms of disease, but the greater number maintain ... present in ... rners among ... tevin (1921) ... er thousand ... the carrier state lasts for two months or more In the acute stages cholera vibrios are excreted by the patient for seven to ten days; more usually they disappear in three or four Y Y Ying (1940) has found, however, that occasionally positive cultures may be obtained for four weeks. ... vo weeks

... nay vary ... estations. The cholera syndrome may supervene upon what appears to be an

who have any intestinal disturbance are more likely to be attacked by the disease than those who have not In most cases the milder symptoms constitute the stage of premonitory diarrhœa and are known

to seventy-two hours from the time of infection.

The onset of true cholera is marked by the sudden evacuation of

sufferer being agonized by these contractions, which cause the muscles to stand out like rigid bars He then passes into a state of collapse

Toxins.—Filtered cultures of the cholera vibrio exert little poisonous action, the virus is apparently liberated by the *breaking up of individual organisms*, and dead cultures, when administered by the mouth, produce little effect unless the intestinal canal is injured in some way. These poisonous bodies are mostly destroyed at 60° C., but, when ground up and frozen by liquid air, an extract is obtained which is extremely toxic if injected intravenously into laboratory animals

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[illegible]

minutes. Should the original culture be that of a true cholera vibrio, the organisms break up into small globules; if not, no change takes place. This *is regarded as the surest proof that a suspected organism is true cholera.*

Pathology.—The appearances found after death naturally vary considerably with the severity and duration of the disease If death occurs in the *algid stage* of cholera, the surface of the body appears shrunken and wizened Rigor mortis occurs early and persists for some time, and, owing to post-mortem muscular contractions, movements of the limbs may take place. On opening the body, all the tissues are found to be abnormally dry The muscles are dark and rigid, and some may actually be found to be ruptured. The right side of the heart and all the main veins are distended with dark, thick, imperfectly

[illegible]

stage of reaction that death may take place from a variety of complications—pneumonia, enteritis, even asthenia—or, more commonly, from

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epidemic are usually milder

The mildest cases are known as cases of *ambulatory cholera*, and are characterized by malaise and diarrhœa These patients never suffer from complete suppression of urine, the diarrhœa never loses its bilious character, and cramps do not occur. Such mild attacks subside without the reaction stage.

Cholera sicca is a very fatal type. In these cases there may be no diarrhœa nor vomiting at all, but collapse sets in so rapidly that the patient, overwhelmed by the infection, dies within a few hours without purging or any attempt at reaction

Hyperpyrexia may very occasionally supervene, the temperature rising rapidly to 107° F in the axilla and to as high as 109° in the rectum Such cases are almost invariably fatal

Special features—During the early days of the acute stage, there is a definite increase in the number of red blood-corpuscles, which may rise to 8,000,000 per c mm At the same time there is an increase of leucocytes, according to L Rogers (1923), an average of 28,000 per c mm is usually met, those cases with a specially high count being generally, but not always, fatal. In the differential count there is an increase in the proportion of polymorphonuclear cells, together with a great decrease in the lymphocytes According to Rogers, the most characteristic feature is the loss of fluid from the blood This has been ascertained by centrifuging defibrinated blood in the hæmatocrit, by which means the relative proportion of corpuscles to serum is ascertained Rogers estimated that in the blood of an Indian there is normally 45 per cent of corpuscles to 55 per cent of serum, but in cholera patients 71 per cent. of corpuscles and only 29 per cent of serum were found, indicating a loss of nearly one-half the fluid from the blood After intravenous injections of hypertonic saline, the normal proportions are rapidly restored Estimations of the amount of chlorides in the blood-serum in cholera show that salt is reduced to a greater proportion than is the fluid. The physiological results of this chloride loss are self-evident

It is on the estimation of the *specific gravity of the blood* that the greatest

solutions are kept in a series of small stoppered bottles The finger tip

Probably owing to dehydration through diarrhœa and vomiting, there is a general shrinkage of the softer tissues; the eyes become

a mere whisper. The circulatory system suffers severely and the pulse soon becomes feeble and thready and, after fluctuating, may disappear. Although the surface temperature of the body is much below normal (it may be as low as 93° or 94° F.), that of the rectum may register from 101°–105°. Restlessness now sets in and the patient tosses about

stage of cholera, and may terminate in death, in a general febrile reaction, or in rapid convalescence.

When death occurs, usually from collapse, it generally takes place within ten to twelve hours of the onset; the extremes are from two to thirty hours. Convalescence is ushered in by a gradual cessation of vomiting and diarrhœa, re-appearance of the pulse at the wrist *and the return of warmth to the surface of the body. Soon,* after apparent suppression for many hours, secretion of urine once more takes place, and in three days or more the patient may be practically well, without any complications. The relationship of anuria in cholera to that of collapse and crush injury, which possess the same physiological background, has recently been emphasized by J. W. Tomb

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It is during this

When the vibrios are present in small numbers, alkaline peptone water should be inoculated with one or more loopfuls of the fluid stool and incubated for seven hours Any pellicle present on the surface of the broth should be [illegible]

[illegible]

laid down by bacteriologists, a considerable amount of time is required, yet it is quite obvious to anyone who has studied the subject that promptness in recognizing early cases of the disease and in identifying carriers is of great importance To meet this need for promptitude, various rapid methods have been devised

Bandi's method consists of inoculating the suspected fæces into peptone water containing the agglutinating serum in such a strength as to clump the cholera vibrios in high dilutions After three hours' incubation, agglutination which is visible to the naked eye will be observed, this is, however, rather a wasteful method, for when employed on a number of cases a large quantity of serum is used

The author, in conjunction with A Davies, employed a modification of this method in Palestine in 1917 and 1918, with apparently satisfactory results. The method consists of agglutinating the vibrio, in peptone-water cultures made from the stools, by small quantities of immune serum on the slide of a Garrow's agglutinometer By this method positive results may be obtained in as short a period as eighteen hours, and as many as two hundred stools may be examined during the course of a morning The following are the stages —

1 A platinum loop full of fæces is inoculated into peptone water (1 per cent peptone, 1 per cent sodium chloride, made distinctly alkaline to litmus)

[illegible]

high dilutions

4 The peptone culture can then be spread with a platinum loop on Crendiropoulo's agar (alkaline agar) and a pure culture obtained by this means The cholera colonies can now be easily recognized by their transparent bluish grey appearance, and hæmolytic and sugar tests can be applied [illegible]

minutes to make, but the data they furnish point the way to accurate treatment.

The *blood-pressure* is also important in cholera and is greatly reduced in the collapse stage. In those cases in which the systolic blood-pressure falls below 70 mm. of mercury, it is necessary to administer intravenous saline injections, in order to maintain the blood-pressure and enable the kidneys to resume their normal functions

Sequelæ.—Cholera may be followed by a variety of sequelæ of more or less importance There may be anæmia, physical and mental debility, insomnia, febrile conditions, chronic nephritis, various kinds of pneumonic consolidation of the lung: even cholecystitis resulting in jaundice. Parotitis occurs in about 1 per cent. of cholera cases and usually ends in abscess formation. Eye complications are frequent and severe; for instance, ulceration of the cornea with slouç [illegible] eyes are kept l [illegible] Bed-sores are [illegible] ıcous membrane of the mouth, toes and fingers has been recorded by older writers Dysentery and diarrhœa may also follow true cholera, but eventually may clear up without much trouble. In elderly and enfeebled people a state of asthenia may develop The danger of sudden cardiac failure must at all times be borne in mind. Pregnant women almost invariably miscarry, and the fœtus shows evidence of cholera infection

Diagnosis.—The diagnosis of cholera on clinical grounds should not, during the height of an epidemic, be particularly difficult. There is the characteristic appearance of the patient, the cold, clammy fingers, the cyanosis, the feeble whisper, the shrivelled fingers and [illegible]

in the stools under the microscope, but it may not be found at the first examination

The usual procedure is for the stools to be microscopically examined. [illegible]

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[illegible]

being pricked, a small quantity of blood is sucked up into a capillary glass tube and then blown into the selected gravity bottle. If it sinks it is heavier, if it rises it is lighter, and another drop is blown into another bottle until the medium is found in which it just floats. These observations take but a few minutes to make, but the data they furnish point the way to accurate treatment.

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Diagnosis.—The diagnosis of cholera on clinical grounds should not, during the height of an epidemic, be particularly difficult. There is the characteristic appearance of the patient, the cold, clammy fingers, the cyanosis, the feeble whisper, the shrivelled fingers and toes, the cold breath, the suppression of urine—all these are sufficiently distinctive. It is in the minor manifestations, the doubtful cases, and the carriers that scientific methods of diagnosis must be employed.

In true cholera the comma bacillus, or vibrio, may be recognized in the stools under the microscope, but it may not be found at the first examination.

The usual procedure is for the stools to be microscopically examined. If the vibrios are present in large numbers, they may be detected by their movement in a hanging-drop preparation, or by their characteristic appearance in films stained by carbol fuchsin. Koch considered that in 50 per cent. of cases diagnosis could be made by this method. When the vibrios are numerous, plates may be spread by means of a platinum loop on Dieudonné's medium, the alkalinity of which possesses the property of preventing, to a great extent, the growth of organisms other than the cholera vibrio. The colonies may then be recognized by their characteristic appearances.

	Cholera	Food-Poisoning
Stools	Rice-water and copious	Liquid but fæcal and offensive Never colourless or copious
Urine	Complete suppression	Never suppressed
Muscular Cramps	Constant Severity depending on the amount of fluid lost from the tissues	Present only in very severe cases. Often associated with tingling and numbness Mild and confined to the extremities
Collapse	Frequent, chiefly from loss of fluid	Never from loss of fluid In severe cases faintness or syncope may occur from toxæmia
Fever	Surface temperature below normal	Axillary temperature 99-102°, accompanied by shivering in severe cases
Headache	Absent	Frequent

Mushroom poisoning produces symptoms resembling food-poisoning; it is dealt with on p 473

Algid or choleraic malaria may simulate cholera very closely, and during the 1914-18 War the author saw many cases of this condition about which a scare of cholera had been raised amongst the troops (See p 268) Subtertian malarial attacks are often accompanied by choleraic symptoms, the stools suddenly become loose, profuse and numerous, but they are not nearly so copious as the rice-water material which pours from the patient in true cholera The diagnosis is confirmed by means of a microscopical examination of the blood and discovery of the subtertian malarial parasite

Acute bacillary dysentery may be so sudden and severe in its onset as to resemble true cholera, and epidemics of the former disease have actually been officially mistaken for the latter. (See p 60)

Acute *arsenical and mercurial poisoning* may also closely resemble cholera, but as a general rule vomiting is the most urgent symptom As in cholera, a leucocytosis may be produced with a high proportion of polymorphonuclears Generally in these cases a history of poisoning can be substantiated.

Fireman's or stoker's cramp occurs in those employed under conditions of excessive heat and moisture, such as are found in the engine-rooms and stokeholds of ships in the tropics, especially in the Red Sea The sufferers excrete frequent watery stools and suffer from marked collapse and severe muscular cramps; these cases thus bear a considerable resemblance to chol[illegible]

In acute *trichiniasis*, a disease which is fortunately becoming far less frequent, gastro-intestinal irritation is produced at the stage when the adult worms in the small intestine reach sexual activity Abdominal pain, vomiting, and severe diarrhœa of the choleraic type may ensue,

factory method of making a diagnosis in true cholera, for an agglutination reaction is not obtainable in the blood serum during the acute stage of the disease; it is present after eight to ten days from the commencement, reaching its maximum in four weeks, when it may attain a titre of 1 : 1000.

Differential diagnosis.—The conditions from which cholera has to be distinguished, and the main point of investigation in each case, may be tabulated as follows:—

Symptoms referable to the gastro-intestinal system	
Food poisoning	History of patient
Choleraic malaria	Blood examination for malaria
Acute bacillary dysentery	Cell exudate in stool
Acute arsenical and mercurial poisoning	History
Mushroom poisoning	History
Summer diarrhoea of children	Character of stool
Symptoms referable to pains and cramps in limbs	
Fireman's cramp	History of patient
Trichiniasis	Leucocytosis and eosinophilia

In other forms of diarrhoea, it has been pointed out that it is rare for the stools to remain as persistently free from bile as they do in cholera. A careful inspection of the stools may yield useful information in other ways. In mushroom poisoning fragments of the fungus may be recognized, and in acute trichiniasis the adult trichina may be identified by the microscope. In choleraic malarial attacks, the spleen is enlarged and the subtertian parasite may be demonstrated in the blood stream.

True cholera has to be differentiated from ptomaine or *food-poisoning*, which may simulate it very closely, but in food-poisoning there is usually a history of several persons being attacked at much the same time after having eaten some article of food. It is said that a great point in the differential diagnosis is that a leucocytosis is present in the early stages of cholera, but absent in food-poisoning. J. W. Tomb gives the following useful differential table between these two conditions.

TABLE XIII

	Cholera	Food Poisoning
Diarrhoea	Painless. Precedes vomiting	Associated with severe abdominal pain; generally follows vomiting
Vomiting	Causes no distress. Watery, copious and projectile. Follows diarrhoea	Often violent and distressing. Vomit consists of food and is never watery, copious or projectile. Generally precedes diarrhoea
Nausea	Absent	Constant
Tenesmus	Absent	Common

massage with the hand or by rubbing in some liniment. Sometimes small injections of morphia are necessary, sometimes chloroform inhalations have to be resorted to. The body should be kept dry by wiping with dry cloths, and the surface heat should be maintained by hot-water bottles placed about the feet, legs, and flanks On no account should the patient be allowed to get up to pass his stools, and a warm bedpan should be provided for this purpose The foot of the bed should be raised. It is necessary that all solid food should be withheld while cholera is active

Essential oils.—A popular and well-established method of routine treatment in India in village epidemics, where scientific methods are not readily available, consists of a mixture of essential oils containing aniseed, cajuput and juniper, which is made up as follows .—

℞ Sp æther	30 ♏
Ol anis	5 ♏
OL cajuput	5 ♏
Ol junip	5 ♏
Acid sulph aromat	15 ♏

[illegible]

place within seven hours of the onset Vomiting, purging, and intestinal distress appear to be immediately controlled

[illegible]

quantities appears to act well, but three or four pints may be necessary If the veins are difficult to find, the injection of saline may be made into the peritoneum or into the muscles of the breast It is said that after a preliminary introduction of two to four pints of normal saline solution into the peritoneum, the superficial veins become prominent, and intravenous injections become practicable. Owing to their collapsed condition it is usually necessary to cut down on to the veins to insert the needle and cannula

Rogers's treatment is based upon the physical conditions underlying the chief symptoms—the blood-pressure, the specific gravity of the blood, and the loss of salt from the body Already in 1898, A J. Wall, considering the routine treatment of cholera by castor oil and calomel to be mischievous, advocated intravenous injection of 0 4 per cent of sodium chloride and 0 2 per cent of sodium bicarbonate dissolved in sterile boiling water He made a practice of stopping the injection when the pulse was restored In moderate cases this took place after the injection of 70 ounces, and in severe ones, after the injection of 5 pints

with muscular cramps and pains. There is usually pyrexia with a leucocytosis and high eosinophilia. Supplementary measures are the intradermal and precipitin tests whenever they are available.

TREATMENT OF CHOLERA

The principles of treatment of cholera may be tabulated as follows:—

Measures controlling efficacy of treatment:

Specific gravity of blood; blood pressure; estimation of the urinary flow; body temperature.

Therapeutic measures.

Hypertonic saline; intravenous sodium bicarbonate; intestinal disinfectants, potassium permanganate; Tomb's essential oils; kaolin.

During cholera epidemics it is most necessary that every case of diarrhœa should be efficiently treated, and for this purpose it has been customary to establish small depots where sedative and astringent remedies are dispensed. Chlorodyne, 15-20 drops twice daily, has been found to be of value in stopping the progress of the disease. *In the early stages of true cholera diarrhœa, opium is of undoubted value,* and a hypodermic injection of morphia ¼ grain, together with atropine 1/100 grain, should be given immediately. With the morphia, the following anti-diarrhœic mixture is of value.—

℞ Sod. bicarb.	15 gr.
Cret. prep.	15 gr.
Sp. æther.	15 ♏
Sp. ammon. aromat.	15 ♏
Tinct. opii	30 ♏
Aq. chlorof. ad	1 ℥

One fluid ounce of this should be given every twenty minutes until the vomiting or the diarrhœa ceases.

Kaolin.—The exhibition at this stage of kaolin or "bolus alba," as an intestinal astringent which at the same time adsorbs the cholera toxins, has many advocates. It was first used by Stumpf in the Serbian [illegible]

General measures.—The patient must be kept warm, in a horizontal position, in a well-ventilated room. Thirst should be treated by [illegible] water, champagne, or brandy [illegible]

massage with the hand or by rubbing in some liniment. Sometimes small injections of morphia are necessary, sometimes chloroform inhalations have to be resorted to. The body should be kept dry by wiping with dry cloths, and the surface heat should be maintained by hot-water bottles placed about the feet, legs, and flanks. On no account should the patient be allowed to get up to pass his stools, and a warm bedpan should be provided for this purpose. The foot of the bed should be raised. It is necessary that all solid food should be withheld while cholera is active.

Essential oils.—A popular and well-established method of routine treatment in India in village epidemics, where scientific methods are not readily available, consists of a mixture of essential oils containing aniseed, cajuput and juniper, which is made up as follows:—

℞ Sp. æther	30 ♏
Ol. anis	5 ♏
Ol. cajuput	5 ♏
Ol. junip.	5 ♏
Acid. sulph. aromat.	15 ♏

[illegible]

distress appear to be immediately controlled.

[illegible]

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General measures —The patient must be kept warm, in a horizontal position, in a well-ventilated room Thirst should be treated by ... soda water, champagne or brandy

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Wall's methods were adopted and modified by Sir Leonard Rogers on the following lines :—

1. The specific gravity of the blood should be estimated to determine the loss of fluid from the bowel, both as a guide to the necessity for administering the saline injection, and as a guide to the amount to be given This estimation should be repeated regularly every morning and evening, and also whenever signs of collapse occur A rise to 1062 is an indication for a saline injection, which, if given early, before actual collapse has taken place, will prevent the development of a serious condition.

2 The blood-pressure should be estimated at the same time, since a fall to a dangerous degree, i e , below 70 to 80 mm in Indians, or 80 to 90 or [illegible] n if

[illegible] to

[illegible] sio logical point This is done to retain the fluid in the blood-vessels and to maintain the blood-pressure and circulation, thereby leading to excretion of the toxins from the system

4 A certain amount of alkali—bicarbonate of soda—is given with the salt [illegible] acidosis

[illegible] istered

[illegible] formed

[illegible]

7. The blood-pressure and the amount of urine being excreted should be watched and all available means employed to maintain the blood-pressure at a level which will ensure free renal secretion.

It is probable that the more modern continuous-drip intravenous saline method holds out greater possibilities in the treatment of cholera.

[illegible]

blood-heat. The low surface-temperatures seen in cholera patients are largely due to deficient circulation, and this is instantly restored to normal by the intravenous injections of salines at blood heat. The hypertonic saline which is most favoured for this purpose is composed as follows :—

℞ Sod chlorid.	120 gr.
Pot chlorid	6 gr
Calc chlorid	4 gr.
Sterilized water	1 pint

The rule now adopted is that the fluid in the containing bottle should be at temperature of 100° F. if the rectal temperature is below 99° F. If the

latter is above 100° F. there is a risk of hyperpyrexia and the injection should be given at a temperature varying between 80° and 90° F

The solution is introduced by means of a special stopcock cannula and transfusion bulb at a rate of not more than 4 ounces a minute, the flow being slowed down to 1 ounce a minute should distress or headache supervene.

[illegible]

It is now becoming increasingly evident that rapid and lasting effects on the restoration of the circulatory equilibrium are more likely to be obtained by the physiological method of transfusion with plasma, or the more recently elaborated reconstituted plasma · the latter is eminently *suitable for the conditions in which cholera is usually found*

Permanganate of potash.—The routine administration of permanganate of potash has received a very considerable amount of support In cholera the alimentary tract is so completely cleared of [illegible]

is to give the patient permanganate solution to drink *ad libitum* in place of water, if he can retain it Owing to the intense thirst in the [illegible]

coloured green The pills are made up of finely powdered potassium permanganate, 2 grains, kaolin and vaseline, q s , and are coated with salol one part and sandarac varnish five parts, or with keratin It is essential that they should not be kept long, for they decompose

Bacteriophage in the treatment of cholera.—In recent [illegible]

choleraphage within 1 and 12 hours of the onset, found no appreciable difference between those treated by bacteriophage alone and those receiving

combined treatment with hypertonic salines, but there was marked improvement in the subsequent incidence of cholera amongst contacts as compared with controls. S. K. Chatterjee and L. R. S. Deo (1938) assert that the [illegible] dministration must be [illegible] nant phage is of the A [illegible] It is this phage which [illegible]

Anticholera serum.—B. Ghosh has published several papers on the use of a new anticholera serum with increased potency, made by a method of toxin production and prepared with the object of procuring a maximum [illegible]

The intravenous route for injection of serum does not produce such favourable results.

Treatment of the stage in which copious evacuations occur.—The great majority of cases come under the care of the physician at this stage, and it may be taken as a principle that no drugs given by the mouth will be of any value in restoring the circulation, because they cannot be absorbed. Stimulant or astringent drugs become inert. There are several instances of this on record; Macpherson, for example, has recorded the case of a native who swallowed 33 grains of opium and 55 drops of croton oil, yet recovered without a single symptom and without any further purging. In another instance, 22 grains of extract of belladonna, given by the mouth and by the rectum, produced no dilatation of the pupils. [illegible] to restore and [illegible] will [illegible] ice.

Rectal injections of normal saline.—These may be tried in comparatively mild cases, when the large bowel retains its powers of absorption. As long as there is a fair pulse, the patient may be tided over the danger of collapse by frequently-repeated and copious saline enemata. Observations have shown that, when the blood-pressure [illegible] will be absorbed; [illegible]

Intraperitoneal injections—Saline solutions may also be injected into the peritoneal cavity, whence they are absorbed more rapidly than from the subcutaneous tissues. This method is specially useful in children, in whom it may be difficult to find a vein large enough for intravenous transfusion The injection may be performed by means

stilette An incision, half an inch in length, is made with a narrow-bladed knife, just below the navel in the mid-line of the abdomen This position is chosen because the peritoneum, being adherent to the umbilicus, will not strip in front of the cannula, unless first perforated

stage of collapse, when suppression of urine has occurred, A W Sellards has successfully established the urinary flow by giving in addition intravenous injections of 2 per cent sodium bicarbonate The objection to using this salt is that it exerts a lytic action on the red cells *in vitro* and may cause convulsions, but in 4 or 5 per cent concentration it has no hæmolysing effect It is thought that possibly, by sterilizing and heating, the bicarbonate is converted into carbonate, and this is injurious, but Sellards found that by sterilization in an autoclave connected with live steam at 7 lb pressure, this conversion was minimized, so that only 25 per cent. of the bicarbonate was converted into carbonate in one hour

Other methods have been used to re-establish the urinary flow Hamilton Bailey and others have recently recommended the

worthy

being

lso, may

s useful

as a cardiac tonic, and may be given three or four times during the twenty-four hours, a mixture containing 5 minims of tincture of

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... of sodium chloride to ... , about the concentra-

highest mortality-rate is amongst the Hindus, who are largely vegetarian in their diet. It is slightly lower among the flesh-eating Mohammedans, and still lower among the Eurasians and Europeans Cholera

"For native troops coming early under treatment it was 30–45 per cent, in European General Hospitals, 50–55 per cent, and for large native civil populations, 60–65 per cent It must be borne in mind that during epidemics of cholera it is a well-accepted fact that the mortality is exceedingly high at the beginning and progressively

lauded

Prophylaxis.—At the present time little attention is paid to quarantine regulations as a means of preventing the entrance of cholera, because convalescent patients may pass the vibrios in their stools for as long as forty-four days from the commencement In the Naples epidemic of 1911, 90 per cent of the cases were traced to direct contact with patients or healthy carriers; and in the Colombo outbreak of 1926, out of 442 contacts examined, 10 per cent were found to be carriers of the cholera vibrio.

In Great Britain practical measures are relied upon for the exclusion of cholera Under this system only ships which are or have been carrying cholera patients are detained, and then merely until they can be thoroughly disinfected By this method merchants and travellers suffer but small inconvenience and loss, and the temptation to conceal cases has been thereby avoided Any suspicious cases occurring on shore are at once reported to the sanitary authorities and promptly dealt with, and every endeavour is made to prevent the fæcal contamination of the public water supplies

In India, during recent years, the prevention of cholera has been

bathing water

Some authorities consider that the mixture of essential oils, if given in one-drachm doses in half an ounce of water, is a good preventive, and

strophanthus, administered three times a day, may be employed as an adjuvant.

Local stimulation may be applied to the kidneys by means of hot fomentations to
of hyperalkaline
pint of normal sa
to four hours in cases in which the collapse appears to have been overcome but suppression of the urine persists.

Treatment of the reaction stage.—If purging should still persist, large doses of salicylate of bismuth, with a little opium, are useful; injections of digitalin 1/100 grain are given to stimulate the cardiac action. Retention of urine may actually occur; the bladder should be examined for this reason and, if necessary, a catheter should be employed. Should the patient then become constipated, purgatives must be avoided, simple enemas being employed instead.

Treatment of convalescence.—In the absence of complications, and with careful regulation of the diet, cholera patients recover their strength with remarkable rapidity, except the very old or those who have previously been in ill-health. It is specially necessary to permit *no sudden exertion, such as sitting up in bed, for a few days*, as the ... Once, however, a

rapidity with which restoration to health takes place.

Nursing precautions.—It must never be forgotten by those in charge of cholera cases that the discharges are a danger to everyone concerned, and that they may contain the vibrio for as long as forty days after the attack. The germ dies quickly when dry, but it reserves its vitality for many days in damp and soiled linen; it cannot be killed by ordinary cold Therefore, the most strict precautions should be taken to disinfect all soiled linen from cholera cases in a 2½ per cent cresol solution Every care must be taken, also, to prevent contamination of the water supplies or of any drinking vessel

Mortality.—The average case mortality in cholera amounts to about 50 per cent Some epidemics are more deadly than others, and usually the death-rate is greater in the earlier than in the later stage of an epidemic In such an exhausting disease, it is the very young or the very old who show diminished powers of resistance. From statistics given by Rogers (1923) it is seen that fewest deaths occur in the
the mor-
h a high
bjects of
eble, the
danger from cholera becomes increasingly great. In the Indian statistics, especially those from the Calcutta Medical Hospital, the

exalted ones could be given safely, and this was found to produce an immunity to all subsequent methods of infection.

It has since been discovered that a negative phase of decreased resistance to this disease occurs for two to four days after the first dose, but there is little evidence that this enters in an important degree into prophylactic measures. It is important to note that the vaccine must not be kept longer than three months, also that the protection afforded is comparatively short—usually about six months

Haffkine spent many years inoculating over seventy thousand persons with his vaccine. The results he obtained were, on the whole, distinctly favourable, and the value of his method is borne out by subsequent statistics, e g, those obtained in the Balkan War of 1913, in Batavia in 1915 and 1916, and throughout the course of the 1914-18 War in different parts of the world.

The reactions produced by the cholera vaccine are usually mild, and the only people for whom inoculation is contra-indicated are infants under two years, and persons suffering from any gastro-intestinal trouble As at present constituted, the vaccine consists of an emulsion of the organisms amounting to eight thousand million per cubic centimetre. The initial dose is ½ c c, this being followed ten days later by 1 c c.

[illegible]

when oral vaccination was carried out at the height of the epidemic, there were only three cases among 300,000 people vaccinated, whilst in the three million unvaccinated more than six hundred cases were noted

Personal prophylaxis—During cholera epidemics great care must be exercised in preserving general health Dietetic and alcoholic

it is possible that by this means contacts in association with a case can be protected.

Sterilization of water.—The cholera vibrio has been described as being capable of living in fresh water from two to sixty-eight days, and in distilled water as long as twenty days In salt water it may live for a considerable time; one to three per cent. of salt does not inhibit its growth, although 5 per cent. is more effective

Disinfection of wells—In most parts of India the water supply of villages and towns is derived from wells, which are very liable to contamination during cholera outbreaks. It is here that potassium permanganate, in the strength of 60 grains to the gallon of water, appears to be invaluable This strength renders the water pink It should be left to stand until it has been colourless for twenty-four hours, and at the same time all vegetation and aquatic insects, if present, should be removed. Potassium permanganate appears to act

is repeated until the whole is passed into solution

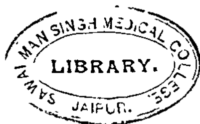
Choleraphage.—Recently J. Morrison has advocated the employment of cholera bacteriophage (choleraphage) as a means of preventing water-borne infection with the cholera vibrio This method has been tested in selected districts in Assam, which, it is claimed, have now been free from cholera for twice as long a period as any during the last ten years.

extended over the Province in an increasing degree

Inoculation.—The present method of inoculation against cholera owes its origin to the pioneer work of J Ferran in 1885. He first demonstrated that guinea-pigs could be protected against lethal doses of cholera by subcutaneous injections of living vibrios After this, over fifty thousand people were ... attack in Spain ... and ... any

In 1892, Haffkine modified Ferran's method of prophylactic inoculation For this purpose he first obtained a very virulent strain of organisms by twenty to thirty passages intraperitoneally through guinea-pigs. For the first dose, an attenuated virus was obtained by cultivating the organism in broth at 39° C. in a constantly aerated atmosphere. A few days after inoculation of this weakened virus, the

The Steatorrhœas



chlorine per million, or 2 grammes of the powder to every 110 gallons)

they may be more likely to contaminate the water than to purify it In households or institutions, abundant quantities of weak tea or lemonade should be provided during a cholera epidemic, the supplies being renewed daily. This ensures the boiling of water in the preparation of drinks Food must be protected from flies.

The Steatorrhœas

CHAPTER XX

PELLAGRA (AVITAMINOSIS B2)

PELLAGRA, a syndrome implicating digestive, nervous and cutaneous systems, must be regarded as a typical avitaminosis Although the digestive phenomena may not always dominate the clinical picture, yet they may play a prominent part, so that it now has claims to be included amongst the " Dysenteric Disorders "

[illegible]

Geographical distribution —Long thought to be confined to Italy, the Iberian Peninsula and the Balkan States, pellagra is now known to have a world-wide distribution It has been reported from Portugal, Spain, S W France, Denmark, British Isles, Germany, [illegible]

bourne *

Epidemiology.—It is probably true that, once recognized in a district, pellagra is generally found to be much more common than was previously considered possible It has long been noted that the number of patients fluctuates markedly from year to year This may be ascribed mainly to dietetic factors but also to the incidence of debilitating diseases which, as is now known, may prove determinative, such as ancylostomiasis, malaria, bilharziasis, tuberculosis, the steatorrhœas including sprue, amœbic and bacillary dysenteries and even syphilis Chronic alcoholism, intestinal tuberculosis, chronic dysentery or operation on the gastro-intestinal tract (gastrojejunostomy or colectomy) may so interfere with normal absorption as to produce secondary pellagra (see p 334)

In countries with marked seasonal variations pellagra appears in an

* For further information see Stannus H S (1936) *Trop Dis Bull* 33, 729

acute and epidemic form
usually the more severe
case In the Northern
appearances are the rule, but in the South it may appear at any season It is probable, however, that climatic factors play but an indirect part in the ætiology

Sex.—Both sexes are liable ; it may be that in different cases it may exhibit a distinct preference for one or other according to local occupation. In the United States, however, it is distinctly more prevalent in women, where domestic work, pregnancy and lactation are considered determining factors

Age.—All ages may be affected, but the majority of cases occur between 20 and 50 *Infantile pellagra is now well recognized and has* been considered a distinct variety It has been reported especially from Italy, America, India, China, and E Africa.

Economic status.—Naturally-occurring pellagra is essentially a disease of the poor and indigent. It is primarily a disease of agricul*tural labourers ; even in the heart of pellagrous districts the urban* inhabitants escape It has been pointed out that it is extremely infrequent in the Jewish race

Ætiology.—Since the days of Lombroso and Bellardini (1871) the occurrence of pellagra has been connected, for apparently cogent reasons, with the consumption of maize, usually diseased It is a fact that pellagra diminished concurrently with improvement in the method of storing and preparing this cereal for human consumption. Hard
... doubtedly also a predisposing factor emphasized
cal
nd
ple
article of diet

W E Deeks and C Funk in 1913 first definitely suggested that pellagra is a diet-deficiency disease, due to lack of certain vitamins, and the latter succeeded in isolating them from yeast and rice. The experiments of J Goldberger and G A. Wheeler in U.S A. on the experimental reproduction of this disease in humans supported this hypothesis. The pellagra which was extremely prevalent in Turkish

were able to identify the PP factor with a vitamin which differed from the antineuritic vitamin (aneurin or thiamin) in its distribution and

U S A as vitamin G) is the carboxylic acid of pyridine, prepared by the oxidation of nicotine The amide is known as nicotamide Both these substances have been found to be essential in meat infusions necessary to the growth of bacteria, especially *Staphylococcus pyogenes* and the

plays a part in carbohydrate metabolism

The richest sources of nicotinic acid under natural conditions are yeast, liver, kidneys, milk, eggs, and cheese A colour test is described for its detection in urine which has been found negative in pellagrins,

[d-1-ribityl] isolloxazine)

Probably riboflavin is an enzyme concerned with oxidation processes in the body cells and, in bringing about metabolic changes, it acts in combination with phosphoric acid—in a process known as *phosphorylation*—which is essential for the absorption of fats by the intestinal epithelium of the villi of the small intestine (see p 353) It is now thought to be associated
and associated diseases,
and the nasolabial fold
rosacea and rosacea inte
thesized by the human organism The rat anti-dermatitis factor (B_6) is now thought to be distinct from the PP factor A pellagra-like disease in rats is caused by deprivation of this substance which is found

to observe on account of the frequency of complicating diseases, such as malaria, ancylostomiasis, chronic bacillary and amoebic dysenteries and occasionally intestinal tuberculosis According to modern conception, all these should be regarded as predisposing factors Great emaciation is constantly observed The viscera show chronic degenerative changes, such as fatty infiltration, and characteristic deep pigmenta-

acute and epidemic form in the spring and autumn, the former being usually the more severe In the southern hemisphere the reverse is the case In the Northern United States, spring and autumn cyclical *appearances are the rule, but in the South it may appear at any season* It is probable, however, that climatic factors play but an indirect part *in the ætiology.*

[illegible]

determining factors

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emphasis that, even if one clinical syndrome dominates the picture, multiple deficiencies are generally present. This applies to deficiency states conditioned directly by ingestion of insufficient diet, or indirectly by failure in digestion and absorption

The Plummer-Vinson syndrome, which has been described in middle-aged women, has many symptoms in common with pellagra Pink disease in children, which is probably an avitaminosis, may also be mistaken for it, as may also lathyrism and ergotism

Under the name of "crazy pavement skin eruption," L Nicholls (1940) refers to a condition common in Ceylon, and indeed in all emaciated natives, especially in Indian seamen (personal observation) Described originally by C D Williams (1933) it is common in otherwise healthy children in Tanganyika (A MacKenzie, 1941) There is a

urine In exceptional cases the diagnosis may have to be made by a process of exclusion

SYMPTOMATOLOGY

Pellagra is a disease, as A D Bigland (1920) so aptly remarked, "difficult to diagnose and often overlooked unless the possibility of its occurrence is kept in mind" It has often been emphasized that in the

pellagra or the *formes frustes* of Stannus

Pellagra is usually drawn out, it does not run a stereotyped course, but is liable to exacerbations and remissions

Prodromal —The initial symptom may be a combination of psychical and digestive disturbances and recur for years in the absence of the typical dermatitis *Larval pellagra* (or pre-pellagra) manifests itself by anorexia with dyspepsia, mental depression, often neurasthenia, constipation and occasional attacks of diarrhœa A sore mouth with

full development

Gastro-intestinal symptoms —

tion.
and di
inflam
the lat
phic changes in the suprarenals were also observed by the author during the last war (1916).

... stated that there are no alterations in the meninges,
esemble those of a chronic
cells exhibit chromatolysis,
hromatolysis of the cells of
Clarke's column Similar changes, but of lesser degree, are seen in
... lesions

disease.
Frequently the rash has at first been confused with some fungus
... syphilis

The nervous manifestations may have to be differentiated ...
hysteria, melancholia, general paralysis of the insane and cerebral
... cases, and in view of the
pon those of
occasionally
ite diagnosis
coming more
may be ...
and more recognized that multiple vitamin deficiencies in man are the rule rather than the exception Davidson has pointed out with some

process appears to be arrested, but the following spring the dermatitis

[illegible]

in the mouth and tongue

Obstruction to the sebaceous ducts on the nose and alæ nasi produce a peculiar sulphur-flaked appearance of the skin which varies in different races, and it is to this that Stannus has applied the term "folliculitis"

Œdema is usually present, it may be universal, as in nutritional œdema, and was common in the series observed by the author and A D Bigland in Egypt (1920) It is found especially in the lower extremities, and is then reminiscent of a similar œdema in cardiac beriberi

Nervous symptoms.—Implication of the nervous system manifests itself by tremor of the tongue and face muscles, by exaggerated reflexes and often by mid-dorsal spinal tenderness Muscular cramps are common The patient is the victim of either insomnia or uncontrollable somnolence He is conscious also of great weakness, especially of the lower extremities Chvostek's sign is usually present Depression develops into melancholia, maybe with maniacal interludes, with a tendency to suicide Finally the pellagrin becomes emaciated, paralysed completely demented and bed ridden and generally dies from diarrhœa, urinary incontinence, exhaustion or intercurrent disease

[illegible]

(1938) have shown that the amount of porphyrin in the urine is directly proportional to the nicotinic acid intake. The derivation of this porphyrin is a matter of debate As pointed out by L Rau (1940), there are cases of congenital porphyrinuria with photosensitive skin lesions not connected with pellagra Porphyrinuria may be referred to hypersensitivity to nitro- and amino-bodies produced by the intestinal dysfunction, or possibly associated with increased destruction of blood pigments

Infantile pellagra.—Recently much has been written about

[illegible]

races

are rigid and painful. Usually there is gaseous diarrhœa and occasion-

diseases. This was noted by C. G. Manning (1909) who referred to
pe

uncommon in native races (de Langen), and yet pellagra is apparently as rare amongst them as is pernicious anæmia)

pellagra is irregular in in-
be established between its
between the occurrence of
anæmia, achylia or diarrhœa (cf also sprue). Not only is the degree, but also the type of anæmia irregular, it may be slight, hypo- or

being secreted by the stomach

although the affected skin

Alcoholic pellagra.—In the northern portion of the United States alcoholic pellagra has been recognized as not uncommon. The term

peared within two to six weeks after drinking crude whisky with little more than a plate of soup a day. Two had delirium tremens. The pellagrous rash appears on the hands and face, but never on the feet.

Pellagra in the insane.

Mental Hospitals, stated that, though in some cases the disease was present on admission, in the majority it appeared after six months' to several years' residence.

Treatment of Pellagra

It is generally conceded that great advances have been made in recent years in the treatment of pellagra. These have been so important

rich in proteins and vitamins. Liver and yeast were regarded as

These children are vexatious and irritable, the skin and hair tend to lose their normal colour and sheen. There are usually gastro-intestinal symptoms with diarrhœa and transient œdema of the hands and face After ten days pigmented patches of dermatitis appear around the ankles, knees, wrists and elbows, especially (it has been emphasized) at the points of *irritation or of pressure. Trowell described infantile* pellagra as a syndrome whose principal signs are œdema, dermatitis and diarrhœa in infants, it has been known as "William's Disease" (Kwashiorkor, W Africa), nutritional œdema with pellagra; *Culebrilla* (ringworm disease) in Mexico, pellagroid-beriberi (Cuba); *Cachexia hydrique infantile tropicale* (Salvador); œdema of avitaminosis (Costa Rica) It occurs as an endemic disease Sporadic cases have been noted in U S A, China and under war conditions in Europe. Acute

[illegible]

(aneurin) Three out of seven cases make a good recovery on nicotinic acid.

"Pellagra typhus."—In this acute and fulminating form there is high pyrexia, prostration, muttering delirium, pronounced nervous tremors, generalized rigidity and not infrequently epilepti-form convulsions *Death may take place in as short a period as three weeks*

Pellagra due to voluntarily restricted diet.—A number of authentic instances have been recorded and collected by Stannus They are most interesting as proving that the disease can be produced by withholding the extrinsic factor, or factors, from the diet. All cases

[illegible]

Secondary pellagra is now generally acknowledged to be a definite clinical entity. In all its manifestations pellagra is connected with some organic lesion of the gastro-intestinal tract. The following is a list:—œsophageal stricture, carcinoma of stomach, carcinoma of the alimentary tract, especially of the transverse and descending colons, ulceration of colon, pyloric ulcer and stenosis after operation for gastric ulcer, *duodenal feeding, carcinoma of head of pancreas and of ileum,* stricture of jejunum, tuberculous enterocolitis, stricture of rectum (lymphogranuloma inguinale), polyposis, rectovaginal fistula, multilobular cirrhosis of the liver and diaphragmatic hernia.

CHAPTER XXI

SPRUE AND HILL DIARRHŒA

Synonyms.—Psilosis, Aphthæ tropicæ (German), Athrepsie coloniale atrophique (French)

The term "sprue" has long been used in the Netherland Indies as

"spruw," has no apparent relation to tropical sprue

Many are the names which from time to time have been bestowed on tropical sprue —Aphthoides chronica, impetigo primarum viarum (Hillary 1766), Indische spruw—aphthæ tropicæ (Van der Burg), psilosis linguæ vel mucosæ intestini (Thin 1897), cachexia aphthosa, stomatitis intertropica, and aphthæ orientalis It was known to the older generation of Indian physicians as white flux, white purging, white chronic diarrhœa, scorbutic diarrhœa, or chronic enteritis of Indo-China In Ceylon it is still popularly termed "sore mouth," in Malaya "Singapore sore mouth"

Definition—The name sprue is given to a tropical and subtropical

sphere in persons who have previously resided in the tropics

History.—Although sprue was recognized as a distinct disease and given a great variety of names by the earlier physicians who practised in India and the Dutch East Indies, the first accurate description is undoubtedly that given by Vincent Ketelaer in 1669, in a work which was reprinted several times In *Observations on the Changes of Air and concomitant epidemical diseases in the Island of Barbados*, an account of what appears to be sprue is given in detail by Hillary in 1766 The name "sprue" was first applied in descriptions written independently by Van der Burg in Java and Manson in Amoy, China, in 1880

nicotinic acid by the mouth; occasionally 100 mgm. were given intravenously.

pel

A.

reported that ptyalism, Vincent's spirochætal infection of the oral cavity and coproporphyrinuria were similarly improved.

due to their nicotinic acid content

In normal individuals (not suffering from avitaminosis) nicotinic acid produces a histamine effect—increased warmth and tingling—in the face and neck, but occasionally nausea, vomiting and abdominal cramps It is essential that nicotinic acid treatment should be reinforced by a liberal protein diet and maintained for several months. The *minimal dose of nicotinic acid is 150 mgm. a day, but in severe cases* 300 mgm or even 1,000 mgm may be necessary.

In cases with severe intestinal disturbance, where the nicotinic acid may not be absorbed, the injection of a suitable soluble preparation is indicated *Coramine* (diethylamide of nicotinic acid) which has long been used as a cardiac stimulant (2–5 c.c. solution up to 20–50 c c) appears to be equa

Spies (1939) find

carboxylic acids

have also shown that

which is the homo-

While on a hill station in 1923, he suffered from hill diarrhœa In 1924, true sprue symptoms began and ran a very rapid course He was admitted to hospital in London in April, 1925, and died three and a half days later from typical sprue anæmia

[illegible]

intestinal tract The soft timbers are invaded by white ants, or termites, and the fæces of these insects give rise to a fine dust which permeates the atmosphere The author investigated this problem during his work in Ceylon in 1912–14, but concluded that there was not sufficient evidence to connect the dry rot with the regional incidence of the disease in that island The subject has been revived by F P Jepson (1933), who has brought forward further evidence of the apparent connexion between the activities of dry-wood-inhabiting termites and the incidence of sprue, but there the matter ends, because the author has investigated many cases in seamen where the disease has originated on ship-board and in other places where nothing of the sort can occur.

Micro-organisms —For the last thirty years search has been made for some micro-organism which might be the causative factor of the disease Most theories have centred round the possibility of the infection of the intestinal tract by a yeast fungus In 1901 a yeast was described by Kohlbrugge as the possible cause

[illegible]

albicans as a distinct pathogenic species

The prolonged researches of B K. Ashford into the possibility of special species of yeast fungus being the causative factor have been inconclusive

Biochemical investigations and their significance, which will be described later, have suggested to N H. Fairley and others that the phenomena of sprue can best be explained in terms of a metabolic breakdown of the gastro-intestinal tract, characterized by defective absorption in the small intestine in some way connected with defective [illegible]

After the occupation of Annam, the French referred to sprue as "entero-colite endémique de Cochin-Chine" and the writings of Berenger-Feraud, Kelsch and Kiener convey the impression that sprue should be regarded as a sequel to some form of dysentery.

In 1897 G Thin published "*Psilosis or Sprue*," containing a summary of the then existing knowledge, in which he illustrated various lesions of the sprue tongue and gave an accurate description of treatment by milk or fruit diet In 1906 there appeared a valuable summary of knowledge by A G. Rademaker, and in 1908 a monograph appeared from the pen of W. Carnegie Brown.

[illegible]

and bacillary dysentery take the first place, though the evidence that these are necessarily precursors of sprue is not convincing. In a series of two hundred cases in which this point was investigated by the author, a previous history of intestinal infection was found in 40 5 per cent, and amœbic dysentery in 32 per cent.*

Sometimes sprue and amœbic dysentery co-exist in the same patient, as in the following instances :—

A very severe case was seen in a man forty-five years of age who had lost 76 lb and weighed only 120 lb. The general appearance of the patient, [illegible]

An officer returned from Iraq in 1920, and suffered from amœbic dysentery with characteristic amœbæ and cysts in the stools. While under observation, he had an attack of hepatic amœbiasis with a temperature of 103° F. Ten days after the subsidence of these symptoms, typical sprue developed, with a sore tongue. For this he was treated on dietetic lines and made a good recovery Since that time he has suffered from a sprue relapse after twenty years of apparent good health.

[illegible] India as "hill dia [illegible] In the author's ser [illegible] in which the dramatic onset of hill diarrhœa merged gradually into sprue :—

An officer aged fifty-six had spent thirty-six years in India. In 1917, on the North-Western Frontier, he had recurrent attacks of hill diarrhœa which ceased after persisting for four months. Three years later, in 1920, true sprue symptoms with typical mouth and tongue lesions commenced. When seen in 1926, six years later, he was a typical case of sprue

A man aged fifty had spent twenty-one years on the railways in Burma

* Whether these figures are in excess of the normal incidence of amœbiasis in tropical residents is a moot point From such investigations as the author has been able to undertake, it is about the average.

While on a hill station in 1923, he suffered from hill diarrhœa In 1924, true sprue symptoms began and ran a very rapid course He was admitted to hospital in London in April, 1925, and died three and a half days later from typical sprue anæmia

Unhealthy surroundings.—There exists a popular idea in Ceylon and in the Far East generally that sprue originates only in those houses which have been attacked by dry rot. These are notoriously unhealthy and the inhabitants liable to catarrh of the nose, air-passages, and intestinal tract The soft timbers are invaded by white ants, or termites, and the fæces of these insects give rise to a fine dust which permeates the atmosphere The author investigated this problem during his work in Ceylon in 1912–14, but concluded that there was not sufficient evidence to connect the dry rot with the regional incidence of the disease in that island The subject has been revived by F P Jepson (1933), who has brought forward further evidence of the apparent connexion between the activities of dry-wood-inhabiting termites and the incidence of sprue, but there the matter ends, because the author has investigated many cases in seamen where the disease has originated on ship-board and in other places where nothing of the sort can occur.

Micro-organisms.—For the last thirty years search has been made for some micro-organism which might be the causative factor of the disease Most theories have centred round the possibility of the infection of the intestinal tract by a yeast fungus In 1901 a yeast was described by Kohlbrugge as the possible cause

Kohlbrugge (1901) found in the intestinal mucus, in the lymphoid patches of the intestinal canal, and in the epithelial covering of the tongue and œsophagus, large numbers of yeast cells resembling *Oidium albicans*, and these organisms were demonstrable in the fæces of sprue patients

In Ceylon (1913) the author found that yeasts could be cultivated from the

The prolonged researches of B K. Ashford into the possibility of special species of yeast fungus being the causative factor have been inconclusive

Biochemical investigations and their significance, which will be described later, have suggested to N. H. Fairley and others that the phenomena of sprue can best be explained in terms of a metabolic breakdown of the gastro-intestinal tract, characterized by defective absorption in the small intestine in some way connected with defective secretion of Castle's intrinsic factor [illegible]

Dietetic deficiency theory.—R McCarrison suggested that sprue might

be a diet-deficiency disease In 1908 Carnegie Brown made the observation that in endemic regions native races are subject to beriberi, and Europeans to sprue, and Elders (1917) postulated that sprue was a deficiency disease. L. Nicholls (1919) supported this hypothesis, and considered that a predisposing dietetic factor was important in the pathogenesis, but that the essential mechanism was a lowered resistance followed by infection Castle, Heath, and Strauss (1931), and Castle and Rhoads (1932) appear to have confirmed that deficient diets frequently antedate the onset of clinical sprue.

The author's theories —Tropical sprue appears to have a definite geographical distribution and throughout its range it appears that the newcomer (i e , the European) is attacked while the indigenous natives for the most part escape , sprue, moreover, appears to have an incubation period ; that is to say, its manifestations do not unfold themselves until after three to six months' residence in the endemic area This [illegible]

mence in individuals who have quitted the endemic area and have lived in Europe for twenty-five or even thirty years It does not, moreover, explain the prolonged latent or quiescent periods

The clinical phenomena do certainly suggest a specific inflammation ranging throughout the intestinal tract and affecting the processes of assimilation , but biochemical researches indicate an affinity, or link, with other allied diseases, such as idiopathic steatorrhœa, cœliac [illegible]

In addition to the vitamins which have already been referred to (p. 829) other factors have to be taken into consideration

Extrinsic and intrinsic factors —In order that normal hæmopoiesis may take place in the bone marrow it is necessary that it should be [illegible]

latter is present in food and is closely related to vitamin B_2, but [illegible] Harris states that, though it has a distribution and heat-stability remarkably like that of the vitamin-complex, it is distinct from riboflavin and nicotinic acid

The extrinsic factor is contained in yeast preparations such as marmite, which is efficient in the treatment of the megalocytic hyperchromic anæmias of tropical sprue and idiopathic steatorrhœa, but ineffective in the similar anæmia of pernicious anæmia, so that it has been suggested that the anæmias which react to marmite and other yeast preparations are due to lack of the extrinsic factor In this

connexion Miller and Rhoads have produced pernicious anæmia in [illegible]

The intrinsic factor of Castle contained in the normal gastric juice of man is thought to be in the nature of an enzyme Meulengracht (1935) has shown that, in the pig's stomach at any rate it is secreted by the pyloric gastric glands and the Brunner glands of the duodenum

The response of glossitis and stomatitis of vitamin B_2 deficiencies to [illegible]

[illegible] nourished peoples in Palestine, Central Africa, India, China, West Indies and south United States

It has [illegible] glossitis a [illegible] therapy [illegible] comparabl [illegible] forward be known as presprue or "larval sprue" (*see* p 331) The author believes that avitaminosis B_2 glossitis is not solely confined to those countries in which nutritional defects are universal and obvious, but may also be encountered in Great Britain It is, for instance, by no means uncommon in patients suffering from intestinal disturbances [illegible]

[illegible] ness of the tongue is found in 61 per cent of pernicious anæmia cases, which approximates to the figure of 75 per cent of the incidence of [illegible] sely [illegible] rac- [illegible] uch [illegible] an [illegible] un- common in tropical sprue But in the latter the absence or otherwise of acid in the gastric juice does not seem to affect the subsequent course of the disease Therefore, in sprue the acidity of the gastric juice cannot be correlated to the absence of the intrinsic factor But in pernicious anæmia this dysfunction is complete and permanent, necessitating con-

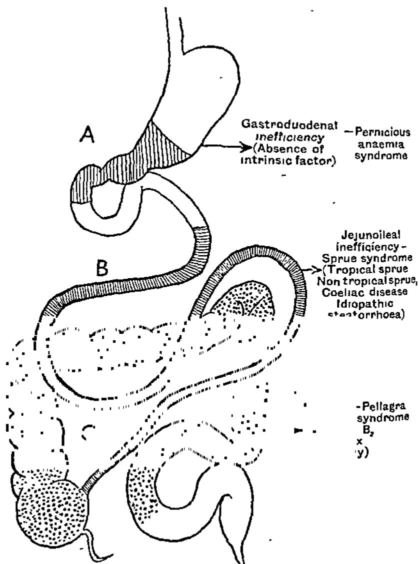

A
B
Gastroduodenal inefficiency (Absence of intrinsic factor)
- Pernicious anaemia syndrome
Jejunoileal inefficiency - Sprue syndrome (Tropical sprue Non tropical sprue, Coeliac disease Idiopathic steatorrhoea)
-Pellagra syndrome
B
x
y)

Fig. 59.

tinuous replacement of the intrinsic factor to maintain health, in tropical sprue it is apparently temporary, so that complete cure is frequently observed without continuous replacement.

[illegible]

glossitis and stomatitis of pernicious anæmia is comparable to that [illegible]

[illegible]

the north in hemisphere This disease is also characterized by glossitis, which is similar to that of sprue and is also amenable to nicotinic acid therapy, though other manifestations do not respond so favourably as in tropical sprue

There appear to be some valid grounds at present for assuming some interconnecting link or common factor bridging the clinical appearances which separate this group of diseases pellagra, pernicious anæmia, tropical sprue and other steatorrhœas. It is possible that the [illegible]

thus it may be evoked by a number of diverse surgical and medical conditions (Fig 59)

blockage of the chyle vessels, as in lymphadenoma, tabes mesenterica or sarcoma of the mesenteric glands.

publication by N. Markoff, wherein it is stated that in two cases in Switzerland typical sprue-syndrome supervened six months after 1.5 m of ileum had been removed (ileocæcal resection with ileo-transverse colostomy).

It is therefore inferred that the main signs and symptoms of sprue may be due to deficient absorption of vitamin B_2 (nicotinic acid) and this appears to be borne out by the results of treatment (p 338) As

important observations upon adrenalin inefficiency in the production of steatorrhœa (*see* p 353).

Geographical distribution.—Tropical sprue is pre-eminently a

Celebes, Macassar, Borneo, Ceylon, and the Philippines, and the author has treated two cases from Mauritius It has been recorded from Queensland, and the Northern Territories of Australia, and a few cases have been reported from Fiji. Sprue has been found in Russian Turkestan Palestine, Mecca, Iraq, Egypt, and Malta In the New

northern Brazil, and appears to be comparatively common in Dutch and British Guiana.

Recently, much interest has been aroused by the recognition of a sprue-like disease in Denmark and Scandinavia generally, which has been designated by Thaysen (1932) "non-tropical sprue" (*see* p 347) which appears to be closely connected with tropical sprue

[illegible]

Jeffreys and Maxwell, in "The Diseases of China," described a typical case of the disease in a Chinaman, and Ashford (1913) in natives of Porto Rico and the Antilles

During the author's work in Ceylon in 1912–14 notes were collected of eleven definitely diagnosed cases in natives Five were recognized immediately before death It was established that the disease occurred, though rarely, in members of several races—in Moors, Sinhalese, Indians, and Tamils who had been bred and reared in Ceylon During the last twenty-one years in London five cases have been seen and treated, mostly in the educated and cultured class of Indians The author has never seen sprue in any member of the negro race

In June, 1929, an Indian lady aged forty was seen, she had suffered from [illegible]

[illegible]

showed no signs whatever of anæmia or sprue, and his weight had increased to 9 stone 1 lb, or by 43 lb

In hospital practice the author has had experience of two cases of undoubted [illegible]

Tientsin in central China Atmospheric temperature alone does not seem to influence its incidence, for it may originate in high altitudes in Ceylon, and in the Himalayas above 6,000 feet, where the climate resembles that of Europe Its occasional occurrence in central Arabia, where the atmosphere is essentially a very dry one, runs counter to the view that a damp climate is a necessary factor in its causation. On the whole, tropical sprue appears to extend for twenty degrees further north than it does south of the Equator (i e. 40°N, and 20°S)

Incidence of the disease in its endemic zones —Sprue is more likely to attack the lighter-skinned races—Europeans first, Chinese and Japanese second, Malays third, dark-skinned Hindus and Tamils very rarely,

occur in one or more members of the same family; the author has recorded instances of sprue in both husband and wife. Moreover, there

convinced that the disease rarely occurs in small children; he has only two instances of sprue under twenty years of age, in boys of thirteen and eighteen respectively. In 1933 R. H Miller demonstrated at the Royal Society of Medicine an undoubted case of sprue in a boy of 11½

fests itself after so long a period that the practitioner is at a loss to associate the train of symptoms with previous residence in the tropics Two instances may be cited —

A medical practitioner, aged seventy-two, returned to England after thirty years' residence in China Symptoms commenced when he had been in

There has been some doubt concerning the length of time which must elapse, after residence in the tropics, before the development of sprue symptoms Formerly it was thought to be a period of years, but evidence has been collected which shows that it may be as short a time as three months, for visitors to Ceylon and India and the Dutch East Indies, who have been there for only a few months during the winter season, and who have never previously resided in the tropics, have returned to England with definite symptoms Two cases may be cited —

The first is that of a boy aged eighteen Symptoms of sprue commenced five months after arrival in Java, with gradual onset of diarrhœa, typical stools, and sore mouth and tongue The total loss of weight was 35 lb , there was complete recovery on appropriate treatment

The second case is that of a woman aged fifty-seven Symptoms of sprue with sore mouth and dysphagia commenced after three months' residence in Ceylon, during her first visit to the tropics Diarrhœa with typical stools and loss of weight followed later, and persisted for six months after her return to England

During the author's studies on sprue in Ceylon in 1912 and 1913, records were obtained of two cases in which the disease began respectively six weeks and three months after the patient's arrival in that island

Sprue contracted at sea —In 1927 the author had under his care a captain of the P & O Line, aged 54 Symptoms of sprue commenced at sea in 1926 when he was fourteen days out from Bombay He had the typical syndrome of sore tongue, aphthous stomatitis, diarrhœa, and anæmia There was little or no evidence that residence ashore had had anything to do with the onset of the disease He had been at sea for forty years, sailing to India and Australia, and during that period he had never spent more than one night ashore in Bombay or any other Indian port He was treated in May, 1927, and reacted very well to dietetic and liver treatment. Four months afterwards he returned to [illegible]

for further treatment of relapses

Non-tropical sprue —The most important contribution to this sub- [illegible]

universal support and the gist of the matter now appears to be that the following clinical states can be recognized :—

1. Cœliac disease in children, a congenital condition
2. Idiopathic steatorrhœa of adults, which probably results from *previous cœliac disease in infancy and which is accompanied by* multiple skeletal changes
3. Non-tropical sprue, a sprue-like disease occurring rarely in temperate and northern countries which is amenable to the same methods of treatment as is tropical sprue.
4. True tropical sprue, the type disease originating in tropical and subtropical countries.

The literature on this subject has now become voluminous and, as may be expected from the intricacies, as well as from the close similarity of the complexes concerned, the issues have become confused. The author is now convinced from his personal experience that very occasionally cases resembling *true tropical sprue, with glossitis, steatorrhœa* and anæmia, may be met with in England and respond to the same methods of treatment in the same manner as tropical sprue. He has records of three such cases The first described (1939) as non-tropical, or "indigenous" sprue was in a woman of 28 years of age who had never been out of England The stools, glossitis, emaciation and anæmia were *typical She suffered from three relapses and eventually recovered* on dietetic treatment Two others were recorded (1940) and responded to nicotinic acid therapy One was in a Pole of 56 who had resided in London for 42 years; the third in a man of 64 who had suffered from recurrent glossitis and stomatitis with steatorrhœa and anæmia for eight years and who had only once been out of England: to Egypt *fifteen years previously Bennett and Hardwick (1940)* have also recorded two cases which seem to fall into the same category. In none of these were there any bone or skeletal changes and the general facies of the disease was identical with that of tropical sprue.

Pathology and Pathological Anatomy of Sprue

In patients dying after such a prolonged chronic wasting illness, the pathological changes observed are usually the results of atrophy, and thus do not give a picture of the actual primary lesions. For this [illegible] elucidate the actual [illegible] have to some extent [illegible] ious anæmia, cœliac [illegible]

In chronic sprue, the tissues are abnormally dry, owing to dehydration, the subcutaneous and visceral fat almost absent, and there is general muscular wasting The internal viscera, also, are shrunken. [illegible] while [illegible] The [illegible] rhaps

remain intact. Somewhat similar fibrotic changes are found in the liver and kidneys

The heart is usually small and in a state of brown atrophy. In the author's series of cases (1912) it weighed less than four ounces, while F. P. Mackie and N. H. Fairley (1929) found that in one of their cases it was only 2½ ounces; they consider this change specific, and the reduction in weight out of all proportion to any decrease explicable in terms of starvation.

Naturally attention has been focused upon the intestinal tract, and

are likely to occur in such a chronic and protracted disease. Knowledge

thick mucus, and occasionally superficial ulceration and pigmented scars of previous lesions have been observed. Death from perforating ulcers has been described by Faber (1904), Fischer and von Hecker (1922) and the author (1924), while Carmichael Low and N. H. Fairley (1934) have reported a fatal case from perforation of the cæcum due to thrombosis of a vein. It is now generally admitted that ulceration of the small intestine may be regarded as a secondary phenomenon.

Although atrophic changes are more marked in the lower end of the ileum, they may
intestine, and diaphar
scopy. It is possible

membranes during life

It may be that the pathological changes in the upper intestinal tract, insignificant though they are to the eye, are of such a character as to inhibit the secretion of the intrinsic factor, and thus be responsible for the macrocytic anæmia of sprue Mackie and Fairley have, for this reason, paid especial attention to the bone marrow changes The red marrow is much reduced in quantity, though in two cases they found hyperplasia similar to that of pernicious anæmia. Their findings suggest that in sprue there is a toxin which primarily stimulates, and later leads to exhaustion of the hæmopoietic function, so that in the terminal stages complete aplasia results.

These pathological studies go to show that sprue is a specific disease of the intestinal tract which leads to progressive degeneration of the absorptive and secretory tissues, and to slow and progressive starvation

Histopathology.—In the microscopic pathology there are very few points of real importance In sections of the tongue, desquamation of the stratified epithelium, especially of the fungiform papillæ, can be demonstrated The same changes are visible in the œsophagus, but often the pathological appearances may be obscured by a downgrowth of yeast fungi (*Oidium*), now regarded as being secondary invaders

The structure of the stomach membrane may be normal, but the intestinal canal, from duodenum to rectum, usually exhibits chronic inflammatory changes. In the ileum the villi are quadrangular and shrunken. The cells stain badly and the goblet cells are distended with *mucous secretion Chronic inflammatory changes are evident in the* [illegible]

[illegible]

in the muscular coats. (Fig. 60)

Sections of the liver show extensive fatty changes in the cells at the periphery of the lobules and deposition of hæmosiderin granules. The [illegible]

membrane of the intestinal canal, and even in the *lymphatic* glands and bone-marrow The changes in the bone-marrow cells vary according to the degree of anæmia present and are well described by F. P. Mackie and N. H Fairley (1929)

Clinical Pathology of Sprue

Stools.—The important features of sprue stools are their colour, size, and chemical composition.

Colour.—It was formerly considered that the large, frothy stools

owed their lack of colour to the reduction or total absence of bile pigments; it is now known, however, that bile pigments are present in normal amounts, but their colouring is masked by an abnormal amount of fat. If the almost colourless sprue stool is extracted with 90-per-cent alcohol, and the filtrate is exposed to the air, colourless fluid results which slowly takes on the yellow colour of hydrobilirubin. That the normal amount of bile is excreted into the gall-bladder is evident from the abundant amber coloured bile found post mortem.



Fig. 60.—Section of the ileum in sprue, showing general atrophic changes and round-cell infiltration of the mucosa.

Size.—The large size of the stool has been variously commented

for the macrocytic anæmia of sprue Mackie and Fairley have, for

suggest that in sprue there is a toxin which primarily stimulates, and later leads to exhaustion of the hæmopoietic function, so that in the terminal stages complete aplasia results.

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The structure of the stomach membrane may be normal, but the intestinal canal, from duodenum to rectum, usually exhibits chronic inflammatory changes. In the ileum the villi are quadrangular and shrunken The cells stain badly and the goblet cells are distended with mucous secretion. Chronic inflammatory changes are evident in the congestion of the capillaries and the infiltration of the interglandular tissue with lymphocytes and plasma cells. There are similar subacute inflammatory changes in the submucosa, and extensive fibrous changes in the muscular coats (Fig 60)

Sections of the liver show extensive fatty changes in the cells at the periphery of the lobules and deposition of hæmosiderin granules The spleen is never enlarged, but shows a deposition of pigment in the pulp cells and hyaline changes in the endothelium of the venous sinuses

and N H Fairley (1929)

Clinical Pathology of Sprue

Stools.—The important features of sprue stools are their colour, size, and chemical composition

Colour.—It was formerly considered that the large, frothy stools

[illegible]



Fig 62.—Section of ileum to show structure of villi.
(Partly after J Schaffer—"Vorlesungen über Histologie," 1924)
(Modified by Verzár and McDougall, 1936)

and peristalsis, the intestinal contents being so hurried through the small intestine that they have no chance of being absorbed, as appears to be the case in some instances of short-circuit of the small intestine which may assume the clinical appearances of sprue On the other

lactoflavin-5-phosphoric acid, depends upon normal adrenal action

these stools goes to show that less than 60 per cent. of the solid matter is absorbed. (Fig 61)

Chemical composition—A great amount of excess fat is passed in the stools, and *pari passu* with this there is a correspondingly low fat-content of the blood (412.8 mgm. per cent. against the normal 600 mgm) N H Fairley finds that in 80 per cent of his cases the total fat in the dried fæces at a single examination exceeded 25 per cent, but after recovery the fæcal fat returns to normal limits In severe cases of



Fig. 61.—Appearance of typical "sprue stool" in glass container.

sprue, over 50 grammes of fat is not uncommonly excreted when the patient is on a mixed dietary In sprue stools the fats are split by the action of the pancreatic and intestinal juices, but the split fat is not absorbed, so that the proportion of fatty acids to neutral fats may be as high as five to one In pancreatic disease, on the other hand, the neutral fats predominate over the fatty acids and may be fifteen times as great. These figures seem to indicate that in sprue the pancreatic digestion proceeds normally, but that the products of this digestion are not properly absorbed The reaction of the sprue stools is almost invariably acid, this is due to the amount of fatty acids, a fact which accounts for the peculiar sour and penetrating odour

Bile assists lipase by —

1 Dissolving fats (neutral and fatty acids) Hydrotropic
2 Lowering surface tension of fat globules and helping to emulsify
3 Enhancing lipase activity about fourteen times

2 [illegible]

This neutral fat is carried to the *lacteals* (via the lymphocytes), from lacteals to the thoracic duct, and thence to the general circulation It is finally lodged in the liver, tissues and fat depots of the body

Bile carries out the physical part of these processes with the actions detailed [illegible]

Hence, there finally appear in the fæces —

Neutral fat	Not digested
Fatty acids Soaps	Not absorbed

Thus, roughly speaking, an increase in neutral fat denotes maldigestion—generally lipase (pancreatic) deficiency, but possibly also bile deficiency to a lesser degree

An increase in free fatty acids and soaps indicates malabsorption—due to bile disease (but here, there will be evidence of maldigestion too, in an absolute increase, though to a lesser degree, of neutral fat), to local bowel disease (cœliac, sprue, etc), or to increased peristalsis Steatorrhœa may be produced in three distinct ways —

[illegible]

(c) Interference with absorption of fats may occur in the mucosa of the small intestine

In the last two contingencies the fæcal fat [illegible]

Adrenal activity is connected with phosphorylation, a chemical process which aids the absorption of fats and glucose Thus, the addition of phosphates in the presence of glycerol accelerates the process, but it can be arrested or entirely inhibited by certain substances, such as mono-iodacetic acid or phlorrhizin Under normal [illegible]

In order to reach a complete understanding of the mechanism of fat-absorption it is necessary to pay some attention to recent physiological discoveries.

The mechanism of ... the small intestine is ... extent of surface produ... *nivventes* They are from 1–2mm. wide and separated from each other by spaces of 1–3 mm and they are widest and nearest to each other in the duodenum and upper jejunum, becoming shorter and thinner until they disappear from the ileum. These are the folds which give rise to the charac... X-rays (p 413) ... the muscularis m... which are long and finger-like, 0 2–1 mm. in height, numbering from 20–40 per sq mm

This mucous membrane is covered by cylindrical epithelium with a striated free border The subepithelial tissues harbour migratory leucocytes, which can pass into the lumen of the intestine, where they ingest bacteria and débris and transport them back to the lymphatic glands

The *lymphatic (chyle) radicles* commence in the apices of the villi, and anastomose (Fig 62) to form a large plexus, communicating with a submucous channel, so arranged with valves that the lymph can flow only in the direction of the lymphatic glands.

The *muscularis mucosæ* is important and is formed of an inner layer of transverse and an outer layer of longitudinal fibres, it extends into the villi

The *mechanics* of fat absorption are important Rhythmical contraction of the villi result in a pumping action, producing the flow of chyle and absorption of fats. They are independent of Auerbach's ... initiated by stimula-

... Local chemical stimula- ... of the villi, and ... tain a hormone

Account of the physiology of fat digestion.

1. Digestion.—*Neutral fat* of food is digested in the small intestine by *lipase* (from the pancreas) assisted by bile and, to a lesser extent, the succus entericus

...

Bile assists lipase by :—

1 Dissolving fats (neutral and fatty acids) Hydrotropic
2 Lowering surface tension of fat globules and helping to emulsify.
3 Enhancing lipase activity about fourteen times

2 ABSORPTION —The products of digestion (glycerin and fatty acids) can now be taken into the lining cells of the villi of the small intestine The bile acids are adsorbed on the mucosal epithelium, so that they are able to dissolve a much greater quantity of fatty acids than *in vitro* (Neutral fat cannot be so taken up) Here, *neutral fat is re formed* This synthesis passes through an intermediate stage of phosphatide formation

> This neutral fat is carried to the *lacteals* (via the lymphocytes), from lacteals to the thoracic duct, and thence to the general circulation It is finally lodged in the liver, tissues and fat depots of the body

Bile carries out the physical part of these processes with the actions detailed above where it acts with lipase

But some of the fatty acids are not so absorbed, and part of the unabsorbed fatty acids unites with bases to form soaps, appearing in the fæces as *free fatty acids and soaps* (about 10 per cent of weight of dried fæces)

Hence, there finally appear in the fæces —

Neutral fat	Not digested
Fatty acids Soaps	Not absorbed

Thus, roughly speaking, an increase in neutral fat denotes maldigestion—generally lipase (pancreatic) deficiency, but possibly also bile deficiency to a lesser degree

[illegible]

be produced in three distinct ways —

(a) [illegible]

(b) [illegible]

(c) Interference with absorption of fats may occur in the mucosa of the small intestine

In the last two cont... [illegible]

specific effect upon the absorptive powers

Adrenal activity is connected with phosphorylation, a chemical process which aids the absorption of fats and glucose Thus, the addition of phosphates in the presence of glycerol accelerates the process, but it can be arrested or entirely inhibited by certain substances, such as mono-iodacetic acid or phlorrhizin Under normal [illegible]

It has further been shown that the presence of vitamin B_2 (nicotinic acid and riboflavin) is necessary for normal fat absorption and that therefore there exists a definite connection between this vitamin and adrenal activity, and on this property probably depends disturbance of fat absorption in pellagra and possibly also in sprue, cœliac disease and idiopathic steatorrhœa. It is therefore apparent that physiological processes underlying fat absorption are more complicated than had formerly been supposed.

Steatorrhœa can be brought about as a result of a break at any point of this physiological chain Only future physiological and pathological investigation can determine where the cardinal lesion of sprue and allied diseases may be situated. It may be (1) in the adrenal cortex; (2) in inhibition of phosphorylation; (3) in absence of the duodenal hormone—*villikinine*—and consequent disordered function of the villi. Whatever may ultimately prove the correct mechanism it appears more than probable that vitamin B_2 plays an essential rôle in linking together these complicated processes

Other considerations in the physiology of the intestine.—Carbohydrate absorption is effected in an easily explicable manner. It is absorbed as monosaccharides, but cane and milk sugar are inverted in the small intestine. the bulk of carbohydrate food consists of starch

[illegible]

... by bacterial action

[illegible]

excessive putrefaction. The average weight of a ... 170 grm.

... features of

The conclusion arrived at by many workers is that a grave degree of anæmia is found in the most advanced stages of the disease. In the

early stages there is no alteration in the number of red or white cells or in their relative proportions, as the disease progresses, however, the former become profoundly altered both in shape and size, and nucleated red cells may appear, though this is rare. On the whole

all probabil[illegible] important [illegible] disease come[illegible] Studies on t[illegible] by the auth[illegible] more recently by N H Fairley, F P Mackie, and H S Billimoria (1929) The conclusions of the last-named workers are as follows —

At the onset anæmia in sprue is rarely found to be so severe as that encountered at a corresponding stage in pernicious anæmia, and during the subsequent course of the disease a grave stage of anæmia less frequently develops As a general rule, grave anæmia occurs with greatest frequency in patients over fifty years of age In about 17 per cent of cases red-cell counts of under 2,000,000 were noted Exceptional cases of 575,000 and 400,000 red cells per c mm are recorded Throughout all the stages of the disease 61 per cent of cases showed a colour index equal to or exceeding unity, while in the

red blood-cells, while poikilocytosis and polychromasia occur but to nothing like the degree usually observed in pernicious anæmia As in the author's experience, nucleated red cells are rarely seen

In uncomplicated sprue, the leucocyte count is either normal or there is a leucopenia usually associated with a relative lymphocytosis A leucocytosis, indicating some intercurrent infection, was observed in only five cases

regeneration which constitute the typical picture of similar crises in pernicious anæmia The Price-Jones curves investigated in eleven cases resembled those obtained in true pernicious anæmia, being

type. The Van den Bergh reaction showed a mean value of 0 66 unit. A comparison between these results and those obtained in cases of malaria and acute pernicious anæmia shows that hyperbilirubinæmia is found more frequently in the two latter diseases; thus the data afforded by this reaction are often of considerable value in differentiating sprue from true pernicious anæmia.

As a result of these investigations it seems that deficient blood production rather than excessive blood loss constitutes the basis of sprue anæmia. The trouble appears to start in an ill-nourished bone-marrow which, poisoned by toxin derived from the alimentary canal, undergoes primary hypertrophy and secondary atrophy.

Serum-calcium and -phosphorus content.—The association of tetany with the chronic diarrhœa of sprue—and, in fact, with other forms of chronic diarrhœa—suggests that there is a calcium deficiency. H. H Scott in 1923 focused attention on the deranged calcium metabolism in this disease, and in 1925 pointed out the value of estimating the serum-calcium in sprue both for purposes of diagnosis and as a gauge of treatment

N H. Fairley, F P. Mackie and F. J. Sacasa (1926) confirmed Scott's observations that the ionic calcium was lowered in sprue readings, 7.4–9 mgm. per 100 c c of serum being constantly registered. E. A. Baumgartner (1927) found in cases of tetany that the total calcium was decreased, readings of 8 1 mgm to 6 2 mgm per 100 c c. of serum being recorded in such cases G. C Linder and T. F. Harris (1930) found that low calcium values (7.8 mgm -7 5 mgm) were associated with a lowered serum-phosphorus content (2 mgm. per 100 c.c.), and that when a low fat diet was instituted the tetany disappeared and the serum chemistry became normal

phosphorus usually varies from 2 to 4 mgm per 100 c.c, no rise above the normal was noted in this series This finding precludes a parathyroid deficiency

As a result it is
factor involved in
stances a low fat
are indicated

Blood-sugar regulation.—In 1926 Thaysen pointed out that in sprue there is an abnormally low blood-sugar curve, a feature common also to cœliac disease (Gee-Herter disease) and other idiopathic steatorrhœas

In these curves the blood-sugar does not rise

the lowest recorded

ises of sprue, Serra

mgm per 100 c c ,

while Fairley and Mackie . mgm per 100 c c

considered that this type of curve is due to an abnormality in the function of the regulating mechanism which maintains the normal blood-sugar concentration, an abnormality possibly due to the disordered function of the adrenal gland

Fairley's recent results (1936) show that in 42 out of 50 cases flat

-us glucose test

ed all showed

d delay in the

he intravenous

glucose curves were always found to be lower and to approximate

ill patients

The blood-cholesterol —This subject has been investigated by H B Newham, R M Morris, and the author (1926) They pointed out

Bombay, and also by the first-named in London The results have been variable For the most part, there is either relative hypochlorhydria or a normal production of acid Out of forty-four cases examined, fourteen showed complete and the remainder a relative

gress of the fractional test-meal, two hours after the gruel had been administered. In thirteen out of eighteen cases a definite secretory response was obtained, while in five there was a true achylia gastrica

accepted, a true achylia gastrica is invariably associated. In the achylia of sprue, histamine response may be regained after proper medicinal treatment In his latest papers Fairley states that in 100 cases only 22 failed to secrete acid when histamine was injected

In the author's series (1941) the after-history shows a variable secretion of hydrochloric acid in the gastric juice and even achylia gastrica Apparently the presence or absence of this acid bears no relation to prognosis.

A. R Olleros (1940) has demonstrated in sprue atrophic gastritis ... and more recently has

the author (1915), the amount of urine passed *per diem* depends upon

urobilin. Indican is present during the acute stages, and apparently depends on the amount of intestinal putrefaction present Urobilin appears intermittently in the urine, especially when the diarrhœa is acute and when there is marked anæmia its presence depends on the

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the diastatic index of the plasma as well as of the urine is greatly increased, and that such an increase may be taken to denote a pancreatic lesion; but, on the other hand, a *normal* diastatic index cannot be

acute

been
(1915).

The former found the saliva alkaline to litmus in the early stages, but acid in the more advanced cases The author found the reaction markedly acid to litmus paper, especially in the advanced stages, the acidity could most clearly be demonstrated on the surface of the tongue and over the inflamed fungiform papillæ In normal subjects the saliva is alkaline or neutral

Summary.—The conclusions which may justifiably be drawn from these biochemical investigations point to the probability that [illegible]

the excess of fatty acids to form insoluble calcium soaps, and this, together with decreased absorption, is possibly the basis of the hypocalcæmia It is certainly a fact that the treatment of tetany by oral calcium is ineffective until the fat content of the stools has been adequately reduced

Symptomatology of Sprue

In hardly any other disease is there such an infinite variety and combination of symptoms as in sprue This applies to the appearance of the patient as well as to the progress of the disease Sprue is really a symptom-complex, there are tongue and mouth symptoms, abdominal symptoms, emaciation anæmia, and lastly the curious mental outlook that accompanies this disease As J Fayrer wrote in 1881, "the appearance of persons suffering from this disease is characteristic They are pale and emaciated with loose, dry, flaccid, flabby skin which in later stages becomes discoloured as by chloasma or Addison's disease The fat disappears, the eyes are pearly, the lips and conjunctiva are blanched, the tongue is dry and smooth and in advanced stages it appears contracted and shrunk There is at last extreme anæmia, dropsical effusions take place into the areolar tissue and the lower extremities" In fact the appearance of sprue patients is so striking that those who are familiar with this disease can recognize it *d'un coup d'œil* (Bertrand and Fontan)

The cardinal symptoms are to be sought in the mouth, the abdomen [illegible]

method of classification of clinical appearances followed in this work [illegible]

[illegible], acute, and chronic *Incomplete sprue* includes a large number of cases in which, though the typical diarrhœa is present, no abnormal pathological changes of tongue or buccal mucous membrane can be

gress of the fractional test-meal, two hours after the gruel had been administered In thirteen out of eighteen cases a definite secretory response was obtained, while in five there was a true achylia gastrica

that in true pernicious anæmia, with which disease, it is now universally accepted, a true achylia gastrica is invariably associated. In the achylia of sprue, histamine response may be regained after proper medicinal treatment In his latest papers Fairley states that in 100 cases only 22 failed to secrete acid when histamine was injected

In the author's series (1941) the after-history shows a variable secretion of hydrochloric acid in the gastric juice and even achylia gastrica. Apparently the presence or absence of this acid bears no relation to prognosis

A. R Olleros (1940) has demonstrated in sprue atrophic gastritis

diminished The reaction appears to be invariably acid, and the urea content normal Interest is centred on the presence of indican and urobilin Indican is present during the acute stages, and apparently depends on the amount of intestinal putrefaction present Urobilin appears intermittently in the urine, especially when the diarrhœa is acute and when there is marked anæmia its presence depends on the

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acute

been
1915).

mucous membrane, the tongue assumes a fissured appearance. It is remarkable how very quickly the filiform papillæ atrophy, while the fungiform papillæ become apparent, standing out pink and swollen [illegible]

[illegible] becomes impossible Swallowing is often accompanied by a sense of soreness and burning under the sternum Dysphagia occurs in about 12 per cent of cases, this very disagreeable symptom being due to excoriation of the œsophagus, which apparently takes place in the same manner as in the mouth *

During exacerbations of the disease the condition of the tongue and mouth become greatly aggravated It is not uncommon to find, however that the mouth [illegible] wh[illegible] tal[illegible] is [illegible] during the exacerbations but shrunken in remissions In a small [illegible]

[illegible] of cases, they usually measure 1–2 mm in diameter and appear to commence in the lower strata of the tongue epithelium as a vesicle, which bursts and develops into small ulcers which are extremely sensitive and very evanescent They have been seen on the inner margin of the lower lip and frænum linguæ, at the tip and sides of the tongue, and on the mucosa of the cheek opposite the lower molars,

* [illegible]

distinguished, but in some of these the typical tongue and mouth symptoms may become apparent as the disease progresses. It cannot be too strongly emphasized that there are rare cases of sprue which terminate fatally without the full picture of the disease being developed. A further subdivision, in which the sprue process appears to be confined to the buccal cavity, may be termed *larval sprue*. These cases are rare and, when observed over a number of years, the more dramatic abdominal symptoms may be found to supervene.



Fig. 63.—Facies of sprue, showing the typical sprue glossitis.

Mouth lesions (Plate XII, 1, facing p. 378)—When the mouth of a typical sprue case is examined, the soreness and tenderness will be found to depend upon a variety of lesions of the mucous membrane which appear to be very superficial. (Fig. 63) It is characteristic that these lesions vary in intensity from day to day During an exacerbation of the disease the tongue appears raw, red, and angry, patches of congestion and minute vesicles appearing on its surface, especially at the tip and sides, in the later stages, owing to swelling of the

the flanks, gives a barrel-shaped appearance In addition, the abdominal wall may become so wasted that it forms a very thin, almost diaphanous

chronic and habitual, the other more acute and, in the early stages,

diarrhœa occurs in the early morning The patient is frequently

formed motions, followed later by violent diarrhœa of an explosive character in acute cases, scalding of the anal margin and of the perianal skin by the passage of so many acid motions may be very

the main abdominal symptoms of sprue

1 *Diarrhœa*	
(a) Early morning	69 cases (34 5 per cent)
(b) Any time of day	116 ,, (58 ,,)
(c) Morning and evening	9 ,, (4 5 ,,)
(d) Night only	4 ,, (2 ,,)
(e) No diarrhœa throughout	1 case (0 5 ,,)
(f) Constipation and diarrhœa alternately	1 ,, (0 5 ,,)
2 *Other Symptoms*	
(a) Abdominal pain	79 cases (39 5 per cent)
(b) Flatulence	144 ,, (72 ,,)
(c) Meteorism	101 ,, (50 5 ,,)
(d) Vomiting	27 ,, (13 5 ,,)
(e) Anorexia	18 ,, (9 ,,)

Shrinkage of the liver —Diminution of the liver dullness was frequently noted by the older observers of sprue as being almost pathognomonic In the series of cases already quoted, a diminution of liver dullness was noted in 56 per cent , and as the result of these observations it was established that the most marked shrinkage was present in the most advanced stage of the disease, usually associated with extreme anæmia

but never on the palate or the fauces. Tongue and mouth lesions were constantly present in about 70 per cent. of cases in the author's series.

Abdominal symptoms.—Dyspepsia is usually a prominent feature, and in some cases it so completely dominates the clinical picture that Manson was originally led to describe this class of case as "gastric sprue." The patient complains of a feeling of weight, oppression, and gaseous distension after eating. Usually the abdomen swells out like a drum; unpleasant borborygmi course through the bowel, and may be audible some distance from the patient. Occasionally this may be relieved by vomiting, which may be sudden and not always accom-



Fig. 64.—Showing meteorism and distension of the abdomen in chronic sprue, with patchy pigmentation.

panied by feelings of nausea; vomiting, however, as a constant feature, is somewhat uncommon in sprue

the author saw a lady suffering from sprue in whom vaginitis was such a distressing feature that it had produced a state of kraurosis.

Meteorism.—Meteorism may be extreme, and in some advanced cases the distended coils of small intestine, especially of the ileum, may be seen *mapped out on the surface of the abdomen, where vermicular* peristaltic waves may be visible. The abdomen is distended, especially below the umbilicus, and this with obliteration of the normal outline of

the flanks, gives a barrel-shaped appearance In addition, the abdominal wall may become so wasted that it forms a very thin, almost diaphanous covering The stomach, also, may be distended with gas and can be mapped out on the surface of the abdomen Extreme dilatation of the stomach is usually associated with tetanic symptoms (Fig 64.)

Diarrhœa.—Diarrhœa associated with sprue is of two kinds, one chronic and habitual, the other more acute and, in the early stages, usually evanescent In the chronic form diarrhœa is characterized by the passage of one or more copious, pale greyish, pasty, and fermenting stools, acid in reaction and of a peculiar sour smell In the acute form it is more watery, but still pale and fermenting, containing masses

character . in acute cases, scalding of the anal margin and of the perianal skin by the passage of so many acid motions may be very distressing Very rarely, in a peculiar chronic form of the disease, the stools have all the characteristics of the sprue stool, but diarrhœa is absent; in others, again, there may be chronic constipation

In a series of 200 cases, the author and Willoughby have tabulated the main abdominal symptoms of sprue

1 *Diarrhœa*	
(*a*) Early morning	69 cases (34 5 per cent)
(*b*) Any time of day	116 „ (58 „)
(*c*) Morning and evening	9 „ (4 5 „)
(*d*) Night only	4 „ (2 „)
(*e*) No diarrhœa throughout	1 case (0 5 „)
(*f*) Constipation and diarrhœa alternately	1 „ (0 5 „)
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(*a*) Abdominal pain	79 cases (39 5 per cent)
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(*c*) Meteorism	101 „ (50 5 „)
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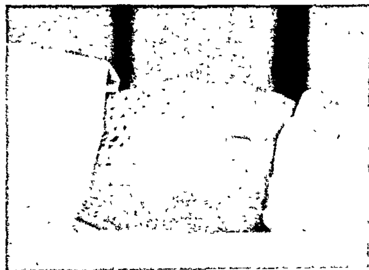


Fig. 64.—Showing meteorism and distension of the abdomen in chronic sprue, with patchy pigmentation.

panied by feelings of nausea ; vomiting, however, as a constant feature,

ay be affected by a In elderly people, common In 1934

cases the distended coils of small intestine, especially of the ileum, may

The blood-calcium was 7 5 mgm per 100 c c of serum, and the inorganic phosphorus 2 4 mgm per 100 c c. of plasma The accompanying anæmia was not extreme The hæmoglobin was 82 per cent., red blood count, 3,000,000; and colour index 1.2 The response to treatment by intravenous injections of calcium gluconate (Sandoz) 5 c c daily for ten days was satisfactory

Skin pigmentation.—A patchy pigmentation of the skin, mainly over face and abdomen, occurs frequently in association with the severe anæmia of sprue Its origin has been discussed by Thaysen, who believes that it is due to some endogenous change and has no relation to adrenal deficiency or to blood destruction (Fig 64)

In Ceylon the author noted pigmented patches, consisting of dark brown areas of irregular freckles on the forehead, temples and cheeks, in the abdomen (in two cases) and on the legs (one case) During the last twenty years, in practice in London, he has noted four other cases. In one lady of 47, from India, who was naturally the subject of leucoderma, the patchy pigmentation of the abdomen was so striking that it resembled the markings on a *Cypripedium* orchid

Larval sprue.—As a rule, the characteristic condition of the tongue is associated with symptoms of gastric and intestinal trouble, but this association is by no means invariable In 1912 the author described a number of cases of Europeans in Ceylon in whom the only manifestation of sprue was the peculiar condition of the tongue, and recently he has encountered other instances of this kind in Europeans treated for [illegible]

the characteristic gastro-intestinal symptoms A typical case may be quoted —

[illegible]

true sprue diarrhœa and secondary anæmia

The recognition of the premonitory or "larval" state in sprue brings this disease into line with pellagra

Special features of sprue in women.—In women amenorrhœa is a very prominent symptom, a feature which has not been adequately recognized It does not seem to bear any close relationship to the development of sprue anæmia, but it has been found to be an early clinical sign The ill-effect of sprue upon pregnancy has long been

Probably this liver shrinkage is but part of the wasting common to the disease

Muscular cramps and tetany.—Cramps are a frequent concomitant of sprue and are present in some form or other in almost every well-

interfere with sleep, passing off directly the diarrhœa ceases.

Tetany of the hands and feet has been noted, in association with the predisposition to cramp, in three instances in the author's series The



Fig. 65—"Tetany" in sprue with low blood-calcium content.

... in spasmodic contraction. Deep

intravenously. (*Fig* 65)

A young married woman was seen in April, 1934, on her return from India after a four years' tour In October, 1933, typical sprue symptoms had commenced, with diarrhœa and later sore tongue and mouth. No diagnosis of sprue had been made in India, in spite of the great emaciation and typical symptoms which she presented On entering hospital, her weight was 91 lb She complained of frequent attacks of cramp in her legs and arms, with tetanic contractions; Trousseau's and Chvostek's signs were both positive

of the limbs and thorax, but there is comparatively little pain or tenderness"

Sprue without diarrhœa—It sometimes happens that cases are met with in which the sore mouth, dyspepsia, and diarrhœa completely subside, but wasting continues, the stools remaining remarkably large—so large that the patient may declare that more is passed in the fæces than can be accounted for by what he has eaten In this condition the wasting becomes progressive and the patient gradually dies On the other hand, the author has met with three patients who passed typical copious sprue motions, without any signs of emaciation or anæmia, and who otherwise appeared to be in good health

Mental disturbances—The mental attitude in sprue is typical, and the whole character of a person may be changed in a curious manner. Those who were formerly reasonable and rational become cross and crotchety, as nurses, sisters, and attendants familiar with the "spruey" temperament know to their cost Usually these idiosyncrasies manifest themselves especially in relation to diet In some cases, particularly where there is considerable anæmia, there may be actual mental derangement The usual psychological state is one of great depression and it is this which makes sprue such a difficult disease to treat. In this respect sprue is distinct from Addisonian anæmia, which it otherwise often resembles As the mental outlook of sprue patients is very often profoundly influenced by the actions of their bowels, their return to good humour on the cessation of the diarrhœa and the more urgent symptoms of the disease is always to be regarded as an index of a return to a better state of health

Anæmia.—The anæmia of sprue has already been described from

diarrhœa has figured as a predominant symptom The blood condition is of importance *pari passu* with the importance of the intestinal symptoms (Chart 11, p 385) The second form is the anæmia which so closely resembles Addisonian anæmia, commencing *de novo* when all the main symptoms of the disease are in abeyance It is this form that is subject to recurring hæmolytic crises

Pyrexia.—In the majority of cases the disease progresses, from the commencement even to a fatal termination, in an apyrexial manner, cases of continued pyrexia due to the uncomplicated sprue process being apparently rare, but fever may occur in sprue as in other severe anæmias, the author has records of ten such cases The temperature may reach 103° F and be distinctly intermittent in character It may be inferred that toxic absorption from the intestinal tract is an important

recognized; it may actually lead to abortion. Usually the sprue symptoms become acute immediately after childbirth.

Complete or typical sprue.—The history given by the majority of patients is somewhat as follows. He has been suffering for months—it may be for years—from irregularity of the bowels and symptoms of indigestion. The diarrhœa usually commences shortly after arrival in the tropics, and for a long time it may be a simple biliousness and early morning diarrhœa. This continues without interfering very much with the general health. Later, the mouth becomes tender, and aphthæ appear for a day or two on the tip of the tongue and inside the lips. If the patient is a smoker, he will notice that pipe-smoking becomes almost impossible. At the same time, there is complete loss of the finer sense of taste. Gradually, the stools lose their bilious appearance and become pale and frothy; the gaseous content may be such that they appear to bubble over. Dyspeptic symptoms, especially meteorism and flatulence, now become apparent, particularly after meals. Anorexia, coupled with loss of taste, is usually complete. As time goes on, the symptoms recur more and more frequently, especially after large meals, severe exercise, or even rapid changes in temperature. *The general condition begins to deteriorate and the* patient is assailed with languor and lassitude, and is unable to get [illegible]

At length the patient is confined to bed. The feet become œdematous and the skin dry, inelastic, scurfy, scaly, and of an earthy tint. Finally the patient dies from heart failure, with choleraic diarrhœa, from inanition, from extreme anæmia, or from some intercurrent disease.

Incomplete sprue.—In some cases all the classical and cardinal signs and symptoms may not be present, as has already been pointed out, these incomplete cases fall into a definite category. In the author's series of two hundred cases they constituted 22 per cent. In this class, the disease process appears to be confined to a limited part of the alimentary canal, thus, a case may proceed to a fatal termination [illegible]

of food, chill, fatigue, or an emotional disturbance brings about dyspepsia accompanied by flatulence and diarrhœa Cases of this sort are prolonged [illegible]

Œdema —A fleeting, generalized œdema has been frequently observed in advanced and emaciated cases when assimilation and absorption have been restored, and the patient commences to put on weight. From the clinical aspect, the author regards this phenomenon as a nutritional œdema or water retention in the lax subcutaneous tissues. Œdema of the extremities is frequently observed in convalescent cases, but passes off when full activities are resumed

General anasarca with ascites has also been recorded in cases of long standing The author has seen two well-marked examples, in which the œdema was definitely of cardiac origin, and was associated with a moderate degree of arterio-sclerosis It cleared up after the exhibition of digitalis

Nerve lesions.—Not infrequently sprue patients complain of paræsthesias—usually a tingling or numbness of the fingers and toes—this being most frequently found in the cases with severe anæmia It has always been considered that serious lesions of the nervous system are absent, this being a main distinguishing feature between sprue and Addisonian anæmia, in which peripheral neuritis and cord degeneration are essential concomitants (L J Witts) Nevertheless, neuritic symptoms associated with chronic sprue have been noted in a retired official from Hong Kong, aged sixty-five years, who had been under the author's care on and off for six years Possibly this may denote a secondary B_1 deficiency

During the whole of this period the sprue process had persisted in a subacute form and there had been severe macrocytic anæmia In spite of the fact that the anæmia had always responded to intramuscular injections of liver (Campolon or Anahæmin), symptoms and signs of neuritis had become apparent There was a persistent tingling sensation in both legs with some paræsthesia, entire loss of ankle- and knee-jerks, and some difficulty on walking It was this disability which caused him to be re admitted to hospital in March, 1938 The response to Vitamin B_1 injections (Benerva 1 c c = 25 mg crystalline Vitamin B [illegible]

ascertainable effect upon the reflexes

[illegible]

jections

factor from the manner in which the temperature defervesces when the patient is placed on a suitable dietary.

Emaciation.—The emaciation of sprue, which resembles that of chronic starvation, exceeds that of almost any other disease, and may be so extreme that the patient loses almost half his body weight. Weight is, however, regained by *means of suitable treatment in* a remarkably short time. The cases here recorded were seen in 1913.

A planter of Ceylon, who had resided in the island for twenty-six years, developed symptoms of sprue, and lost 56 lb in weight within four months. By treating himself in his own bungalow with milk, eggs, and fruit, he eventually regained his normal weight of 178 lb., and when seen three years later was in good health

Basal metabolism.—Very few observations have been made upon the basal metabolism in sprue Such records as exist are by Kassirsky

a tendency to increase, but that this increase may subside as the patient improves under treatment.

systolic blood-pressure was 20 mm. below normal, while the diastolic

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also been noted, with relapses (in the author's experience) after an interval of apparent good health for 20 years, or even longer

COMPLICATIONS* AND SEQUELÆ

Intestinal atrophy consequent upon sprue.—In certain instances the symptoms of sprue disappear, but digestive and assimilative faculties are permanently impaired Slight irregularity in the amount

* It will be noted that many chronic complications of sprue have been found attributable to vitamin deficiencies

tongue at the same time

Bad teeth and pyorrhœa must necessarily be attended to only after the subsidence of the more acute symptoms of sprue. Great care must

anything to do with the genesis of sprue

Co existing infections are apt to complicate sprue, e g, syphilis, *Bacillus coli* infections of the urinary tract, probably due to general debility, malaria, especially the benign tertian form, which may provoke relapses, amœbic dysentery, lung complications such as lobar pneumonia, and acute appendicitis, quite a common complication. The author has also seen a combination of diabetes and sprue, this constitutes an almost insuperable problem, mainly because the dietary that suits sprue aggravates diabetes, and *vice versa*, insulin treatment has proved unsatisfactory There are certain cases of sprue which appear to be complicated by a mild degree of pancreatitis, and in these the exhibition of liquor pancreaticus and pancreatic extracts appear to be followed by good results

The effects of intercurrent disease upon the progress of sprue constitutes a curious, and it may be, a difficult problem The author has seen two cases which recovered completely after passing through a

May, 1932, contracted severe cholera from which he nearly died. Since he recovered he has had no more symptoms of sprue

Skin lesions.—Sprue cases, when responding satisfactorily to

hæmorrhage This is specially likely in those cases which have been continuously fed on an artificial milk dietary The author has had experience of two cases in which a purpuric rash, appearing on the legs

A man of fifty-four, from Hong Kong, who was known to have suffered from sprue symptoms for twenty-one years, was first seen in February, 1927, *in extremis*, with the most severe form of anæmia The hæmoglobin percentage was estimated at 10, and the red blood-corpuscles at less than 400,000 per c mm Following blood-transfusions he made a rapid recovery, and remained well until three years later, when he had a severe relapse for [illegible]

the anæmia and general condition improved, but the signs of subacute combined degeneration became more and more evident, and finally, previous to his return to Shanghai in September, 1932, he presented a typical clinical picture of that condition

Sprue secondary to dysentery and other abdominal diseases.—Some authorities consider that sprue may be secondarily implanted on the bowel which has been previously affected by bacillary or amœbic dysentery. The statistical evidence in favour of this will be found on p 338 Usually the patient gives a history that the motions, formerly characteristic of the original dysenteric attack, have gradually become changed in character. From being scanty, mucoid, and bloody, and accompanied by pain and tenesmus, they become diarrhœic, pale, and frothy, at the same time the mouth becomes sore Hill diarrhœa is a frequent precursor of sprue and in many cases this somewhat trivial complaint merges into the more severe disease.

Intercurrent illness affecting sprue patients.—*A list is given* of the intercurrent diseases encountered in a series of two hundred cases.

Amœbic dysentery	2	Neurasthenia	2
Syphilis	9	Diabetes mellitus	2
Eczema	3	Pyorrhœa	3
Psoriasis	1	Acute appendicitis	5
Pneumonia	2	*Malaria*	4
Alcoholism (acute)	1	Duodenal ulcer	1
B coli infection of the urinary tract	10	Renal calculus	1
		Septicæmia	1
Peripheral neuritis	1	Giardiasis	1
Ancylostomiasis	1	Hæmorrhoids	2
Rectal polypus	1	Scurvy	2

tongue at the same time

Bad teeth and pyorrhœa must necessarily be attended to only after the subsidence of the more acute symptoms of sprue Great care must be exercised in advocating a time in which dental interference may be undertaken, the author has seen too rapid and vigorous extraction provoke a serious relapse It is a mistake to suppose that oral sepsis has anything to do with the genesis of sprue

Co-existing infections are apt to complicate sprue, e g, syphilis; *Bacillus coli* infections of the urinary tract, probably due to general debility; malaria, especially the benign tertian form, which may provoke relapses, amœbic dysentery, lung complications such as lobar pneumonia and acute appendicitis, quite a common complication The

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This feature was first noted by H Werner (1914).

Very often in advanced cases with severe anæmia, numerous bluish-grey subcutaneous patches are noted, especially on the legs, and the patient is liable to bruising after the least injury. These patches were specially noticeable in a female patient from India, aged forty-four, who was treated in 1931 They rapidly disappeared on an antiscorbutic dietary reinforced with adequate doses of calcium lactate. A hæmorrhagic tendency occasionally accompanies idiopathic steatorrhœa which has recently been ascribed to vitamin K deficiency (*see* p. 412).



Fig 66.—Petechial hæmorrhages on the dorsum of the hand in chronic sprue, with extreme atrophy.

Scurvy as a complication of sprue.—A ship's engineer, aged thirty,

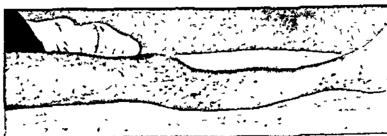


Fig. 67.—Scurvy rash in sprue, showing distribution of petechiæ round hair follicles. (*Vitamin C deficiency*)

Secondary pellagra in sprue yielding to nicotinic acid—

to nicotinic acid (150 mgm per diem for ten days plus 50 mgm per diem for six weeks) was striking The sprue symptoms disappeared and the pellagrous rash faded He increased 18 lb in weight, while maintaining his former dietetic restrictions The history of this case clearly demonstrates that in chronic sprue Vitamin B_2 (the PP factor of pellagra) may be concerned, just as in the case of Vitamin B_1 and Vitamin C (pp 371 and 374) and lends weight to the contention that sprue and pellagra probably are allied diseases

Diagnosis

Differential Diagnosis

Addisonian pernicious anæmia —The differential diagnosis from true Addisonian, or pernicious, anæmia is not always an easy matter In this disease there is achylia gastrica, whereas in sprue there is usually hypochlorhydria with response to histamine (*See* p 359) Sprue exhibits a typical megalocytic anæmia, yet normoblasts are rare and high Van den Bergh serum bilirubin readings—which are the rule in true pernicious anæmia—are exceptional. The stools of pernicious

anæmia are apparently normal There is rarely the degree of emaciation which is seen in sprue—in fact, the body is generally well nourished, and the heart and other organs are not wasted to the same degree The tongue in Addisonian anæmia may be normal or may have undergone inflammatory changes, whereas in sprue the process is more localized (Plate XII, 3); the glossitis in both cases is probably similar.

The syphilitic tongue is characteristic, being distinguished by leucoplakic patches, often deeply fissured and irregular in shape Often small sinuous ulcers or excoriations may be observed, and the submaxillary lymphatic

[illegible]

associated with great sensitiveness, and usually with aberrations in taste.

[illegible]

and is noticeable in the terminal stages of ancylostomiasis

Rough and fissured tongue —An extremely ragged and rough tongue with accentuated clefts or fissures is commonly encountered in native races Both filiform and fungiform papillæ appear to be hypertrophied The author has frequently encountered this form in Europeans, in whom it appears to be hereditary and a family characteristic, usually associated with hyperchlorydria (Plate XII, 6)

Geographical tongue —(Plate XII, 5) is occasionally encountered, and

[illegible]

Tongue of larval pellagra —During his researches in Ceylon in 1912–13, the author described a red raw excoriated tongue over the greater part of which destruction of the superficial epithelium takes place (Plate XII, 2) It was found among prisoners and the inmates of institutions in which salted fish formed the principal article of diet With the raw and red tongue, there is an excoriated and eczematous condition of the angles of [illegible]
plakic condition of the lip
inclined to believe that it
L. Nicholls made further
that it was associated with mild neuritis and definite eye symptoms, suggested that it was due to avitaminosis B_2. Clinical response to nicotinic acid (T. D Spies) has conclusively demonstrated the correctness of this view.

The case of a married woman, aged sixty-two, was (1939) investigated by the author, to whom she had been referred as a case of sprue contracted in South Africa. She had been ill for five years with constant diarrhœa and stomatitis,

weeks

atrophy, in males it was associated with a scrotal rash

Glossitis associated with dyspepsia—This list does not exhaust the tongue changes with which sprue may be confused In grave degrees of dyspepsia associated with gastric hyperacidity, a transient glossitis is often seen In 1936 the auth

0 474 per cent of free hydrochloric acid A barium meal showed gastrospasm, which disappeared after treatment with alkalis and belladonna

Glossitis of diabetes, which is confined to the tip of the tongue, is also sometimes met

Cœliac disease.—From cœliac disease (intestinal infantilism or the Gee-Herter syndrome) the problem of differentiation is by no means easy Cœliac disease occurs, as a rule, in children, and is frequently seen in those who have been reared in the tropics As has

steatorrhœa.

Chronic pancreatogenous fatty diarrhœa.—The differentiation of sprue from this disease is by no means always easy, because in both there are steatorrhœa, emaciation, meteorism, and diminution of the liver dullness, and in both there may be anæmia and occasionally tetany.

In chronic pancreatitis, stomatitis is *absent* and *there is usually no* anæmia. The fæces of pancreatogenous fatty diarrhœa are usually

The enzyme-content of the duodenal juice is normal in sprue, lowered in chronic pancreatitis.

Tropical macrocytic anæmia* (tropical megalocytic anæmia, tropical anæmia of pregnancy) is a severe megalocytic, hyperchromic anæmia of nutritional origin, in which the blood-picture resembles that of sprue. It especially affects pregnant women in the tropics, and responds specifically to the administration of marmite and liver extract,

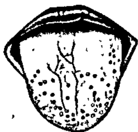
free hydrochloric acid in the gastric juice. Marmite cures this condition, but it has recently been shown that vitamins B_1, B_2 and B_4 are not responsible for this result, the curative factor probably arising from a protein breakdown during autolysis.

Pellagra.—The differential diagnosis between sprue and pellagra may be difficult. In those countries where the two diseases are found side by side, for instance, in the West Indies and in the southern United States, the difficulties may be considerable, and some authors—notably E. J. Wood—have considered them identical. There very frequently occurs in pellagra a sprue-like diarrhœa, but whereas in sprue the stools are excessively large, in pellagra this is not the case. Further,

pellagra affects the nervous system, leading to severe psychoses, and that it is not associated with any severe degree of anæmia. There is, in addition, the characteristic pellagra rash, wherein pigmentation

* It has been suggested that "nutritional megalocytic anæmia" would be a more appropriate term.













P H Manson Bahr del

1, Tongue of acute sprue showing characteristic aphthous lesion. 2, Tongue of B2 avitaminosis and pellagra to demonstrate fissures and rhagades at angles of mouth (painted in Ceylon, 1912) 3, Tongue of pernicious anæmia—the glossitic anæmia of Hunter. Note general atrophy associated with inflammation 4, Tongue of tertiary syphilis, with leukoplakia. 5, Geographic tongue in a girl of twelve 6, Rough, fissured tongue with hypertrophied papillæ—a congenital condition.

DIAGNOSTIC PLATE OF TONGUES

PLATE XII

persists during the quiescent periods, sufficient to distinguish it from sprue (see Table XIV, p. 382).

[illegible]

persistent low blood-pressure of the latter disease (systolic under 100 mm) and its response to injections of adrenalin, also aids in differential diagnosis

Gastro-jejuno-colic fistula may cause fatty diarrhœa associated with glossitis, emaciation and anæmia S Strauss (1921), De Rivas (1930), N H Fairley and T P. Kilner have called attention to the possibility that such a condition may be mistaken for sprue The last-named have described four cases in which some of the symptoms observed in sprue were present—*i e* fatty diarrhœa, emaciation and glossitis, associated with hyperchromic anæmia, in three of the patients gastro-enterostomy had previously been performed (*see* p 340)

Disease of mesenteric glands.—For some time it has been recognized that the clinical syndrome of mesenteric lymphatic obstruction, whether due to tuberculosis or to lymphadenomatous deposits, closely resembles that of sprue.

W. H Allchin (1907) described a clinical syndrome resembling sprue in *tabes mesenterica* In children, he says, besides the fatty and milky stools, "the tongue is red irritable, or denuded of epithelium" Massive tuberculosis of the mesenteric glands is seen mostly in children, and appears to be especially common in Scotland It is usually a primary mesenteric infection, but may be associated with tubercular peritonitis The symptoms consist of wasting, diarrhœa with the passage of light-coloured fatty fæces ; a distended, doughy and hyper-resonant abdomen and in some cases [illegible]

[illegible]

but it is otherwise with adults For instance .—

[illegible]

First impressions suggested sprue with a past history of tuberculosis This supposition was supported by the abdominal meteorism, the pale, bulky stools (14 to 16 oz) containing fatty-acid crystals, and the definite excoriation of the buccal mucosa, with sprue-like inflammation of the tip of the tongue Against the diagnosis of sprue were the facts that the amount of fat in the stools was relatively small (26.7 per cent) and that the anæmia (R B C. 4,000,000, hæmoglobin 70 per cent) was of the secondary type, with a colour index of 0 8. The blood-calcium was, however, low (9 6)

tuberculosis

C W Ross (1936), in three cases of tabes mesenterica in children, found oral sugar curves of the flat type, such as occur in sprue and cœliac disease, and concluded that defective absorption of carbohydrates was responsible.

(p 381). However, in lymphadenoma, palpable tumours or masses sooner or later become apparent in the mesentery, and the stools, though light-coloured and fatty, do not contain the same constant high fat-content as in sprue.

dietary The stools numbered between four and seven a day, and were pale,

N. H. Fairley and F P Mackie (1937) have described a series of four cases of lymphosarcoma in which the clinical syndrome resembled sprue, tongue symptoms, abdominal distension, visible peristalsis, and steatorrhœa being present. Glucose curves in these cases were similar to those of sprue, and were due to defective absorption from the intestinal tract, a factor responsible for the steatorrhœa

Malignant disease of the *small intestine* may also produce a clinical picture of sprue In 1924, J G Willmore described a patient from whom a lymphosarcomatous growth infiltrating the ileum had been removed. The fæces in this case were typically sprue-like, and on analysis contained 53 7 per cent of fat, of which 20 59 per cent was neutral fat and 29 11 per cent fatty acid Signs of intestinal obstruction becoming urgent, an emergency operation was performed, which revealed a malignant stricture at the junction of the upper two-thirds with the lower third of the small intestine, with enlarged mesenteric glands Resection with lateral anastomosis was followed by uninterrupted recovery After operation the fæces became normal in size and colour, and contained 25 23 per cent of fat The patient died two years afterwards from a recurrence

Syphilis.—Differentiation from syphilis affecting the mouth or the bowel is best decided by means of the Wassermann (or Kahn) test, but it must, of course, be appreciated that sprue and syphilis may co-exist in the same patient In the author's series of 200 cases, there was associated syphilitic infection in nine

Radiographic appearances—The radiographic appearances of the bowel in sprue have been investigated by Pillai and Marthi In acute cases there is no indication of the loss of tone or motility in the stomach or intestine The stomach empties in two hours after the barium meal and the intestine in six to eight hours In the subacute condition there is loss of tone and diminution in the peristaltic action In chronic and atrophic cases, the terminal coils of the ileum are greatly dilated, the lumen of the bowel is distended, the outline of the transverse colon is smoother than normal, and marked haustellation is absent These findings agree with those ascertained by routine radiography in the Hospital for Tropical Diseases, London

D K Miller and W H Barker (1937) have shown that the most significant abnormalities are distortion of the mucosal pattern and a variation of the calibre of the intestinal loops Striking changes were observed in the jejunum, the normal delicate feathery pattern being replaced by one of coarser texture The loops of the small intestine were dilated, especially in severe cases Successful treatment resulted in disappearance of radiographic abnormalities This has been confirmed in the main by M Feldman (1938) T T Mackie and M A Mills (1940) also describe as characteristic changes commonly seen in the duodenum and jejunum where the mucosal pattern is coarser than normal with striking variations in contour and size of the lumen In

First impressions suggested sprue with a past history of tuberculosis This supposition was supported by the abdominal meteorism, the pale, bulky stools (14 to 16 oz) containing fatty-acid crystals, and the definite excoriation of the buccal mucosa, with sprue-like inflammation of the tip of the tongue Against the diagnosis of sprue were the facts that the amount of fat in the stools was relatively small (26 7 per cent.) and that the anæmia (R B C 4,000,000, hæmoglobin 70 per cent) was of the secondary type, with a colour index of 0 8. The blood-calcium was, however, low (9 6) and blood-cholesterol 119 mgm per cent

glands were enlarged and showed, on section, the histological picture of chronic tuberculosis

C W Ross (1936), in three cases of tabes mesenterica in children, found oral sugar curves of the flat type, such as occur in sprue and cœliac disease, and concluded that defective absorption of carbohydrates was responsible

Malignant disease.—Lymphosarcoma or lymphadenoma of the *mesenteric glands* may give rise to a clinical picture somewhat resembling that of sprue So may also lymphosarcomatous infiltration of the *lower end of the ileum, as in the case described by J. G Willmore* (p 381) However, in lymphadenoma, palpable tumours or masses sooner or later become apparent in the mesentery, and the stools, though light-coloured and fatty, do not contain the same constant high fat-content as in sprue

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	Pernicious Anæmia	Tropical Sprue	Idiopathic Steatorrhœa	Pellagra (Larval cases common)
Course—cont			Infantilism in severe grades Absorption affected by fat metabolism Tendency to hæmorrhages	Changes in central nervous system resemble subacute combined degeneration Mental symptoms, irritability, excitability, melancholia No osteoporosis, but fragility of bones
Pathology	Megalocytic anæmia, and leucopenia Megaloblastic hyperplasia of bone marrow Bilirubinæmia Blood glucose curve normal Blood calcium normal	Megalocytic anæmia, and leucopenia Bilirubinæmia occasional Flat blood glucose curve Hypocalcæmia Tetany and cramp occasionally Bone marrow atrophic	Megalocytic, hyperchromic anæmia and leucopenia, or single hypochromic anæmia Bilirubinæmia absent Flat blood glucose curve Hypocalcæmia extreme	Megalocytic, hyperchromic anæmia and moderate leucopenia in a proportion of cases Bilirubinæmia absent Blood glucose curve normal Blood calcium normal Urine porphyrins in excess
Treatment	Responds to liver fraction Campolon or Anahæmin, and to some extent to vitamin B_2	Responds to liver fraction, Campolon or Anahæmin intramuscularly in large doses, + vitamin B_2 (Nicotinic acid)	Responds to some extent to liver in large amounts, vitamin B_2 and vitamin D	Responds to vitamin B_2—Nicotinic acid and riboflavin
Relapses	Relapses inevitable, unless reservoir dosage of liver extract is maintained	Spontaneous recovery frequently observed May commence *de novo* in England 25-30 years after return from the tropics	Spontaneous remissions of short duration	Spontaneous remissions tend to occur in untreated cases

* In the author's series the average age of onset is 45 years

TABLE XIV.

	Pernicious Anæmia	Tropical Sprue	Idiopathic Steatorrhœa	Pellagra (Larval cases common)
ge .	40–60 years	20–60 years *	20–60 years	20–50, but may commence in infancy
istribution .	Apparently absent or rare in tropical natives Mostly in well-fed Northern Europeans	Peculiar *tropical distribution*—(Central Africa excluded) Mostly in Europeans and well-fed people	*Mostly Northern Hemisphere*	Mostly tropics and subtropics in ill-nourished people
ause. .	Intrinsic factor absent, does not return on treatment Preceded by achylia gastrica Atrophic gastritis	Intrinsic factor absent, returns on treatment Hypochlorhydria (Achylia gastrica rare) Atrophic gastritis Previous intestinal disease predisposing factor	Allied to, or sequel of "cœliac diseases" in infancy Developmental defect of fat absorption Achlorhydria rare	Deficiency disease of dietetic origin Deficiency of PP factor (vitamin B_2) Frequently secondary to chronic intestinal diseases, such as *intestinal* tuberculosis, bacillary dysentery and sprue Achlorhydria in 40 per cent of cases Achylia rare
ourse .	Onset insidious Glossitis common, dysphagia rare Wasting slight Spontaneous remissions distinct feature Diarrhœa frequent. Bilious stools Peripheral like polyneuritis Changes in central nervous system common (subacute combined degeneration) No bone changes	Onset insidious Glossitis common, dysphagia occasional Wasting extreme Remissions distinct feature Steatorrhœa. Fatty acids, soaps scanty. Whole alimentary tract involved, especially small intestine, megacolon occasional Changes in central nervous system very rare Osteoporosis not observed	Onset insidious Glossitis and dysphagia common Wasting extreme Diarrhœa frequent, steatorrhœa *50 per cent fat mainly split*—soaps Megacolon common Changes in central nervous system uncertain Tetany and cramps frequent Pains in bones—kyphoscoliosis Genu valgum · osteoporosis Fractures Clubbing of fingers, lens opacities	Onset insidious Affected by sun's rays; spring recrudescences Glossitis and dysphagia common Wasting moderate Prodromal symptoms common Diarrhœa frequent, + dyspepsia. Stools, bilious, may be fatty—usually superadded intestinal infection Eruption — dermatitis — hands, face, arms, scrotum—always symmetrical

such as uterine discharges, syphilis, scurvy, dysentery, or helminthic infection, must be dealt with as far as possible The weight of the fæces should be determined daily by weighing pan and contents and subtracting from the total the known weight of the former The *average weight of normal fæces is from six to eight ounces per diem*; in sprue it may be twice or three times this amount By making a

, an estimate may be formed of

blem of diet in sprue is one of

which connexion the reader is

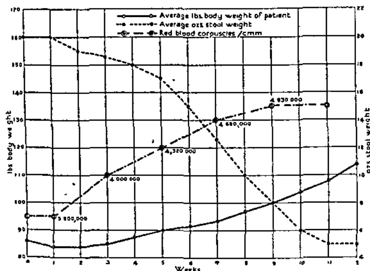


Chart 11.—Composite graph of ten cases of sprue to show the relative increase in body-weight together with the increase in red blood-corpuscles per cubic millimetre and with decrease in average weight of the stool.

Although there are many opinions as to what comprises the most suitable dietary, it is agreed that two principal food constituents—fats and starches—cannot be completely digested or assimilated The introduction into the diet of as much easily assimilable protein as the patient is capable of absorbing is therefore indicated

So many different lines of treatment have been advocated that it becomes a matter of difficulty to decide which is the best There have been fashions in the treatment of sprue as there have been in that of many other long-continued and chronic diseases The modern idea underlying treatment is to place it as far as possible upon a scientific basis, to lay down a scientific diet and adhere to it as much as possible.

the small intestine motor activity is disturbed and there is segmental distribution of the barium in dilated coils (*see also* p 413). These abnormal appearances can be reasonably explained by physiological changes in the small intestine

Sigmoidoscopic appearance of the bowel in sprue.—The
prue in the acute
ormer the mucous
our, with absence
mucosa. In the

are either suppressed or evanescent

The sprue process commonly extends into the large intestine; indeed it may affect the mucous membrane of the whole tract. The changes seen in the upper rectum may then be taken as an indication of the pathological appearances throughout the intestinal tract. Often, too, the characteristic pale, wax-like, semi-solid fæces may be observed pouring down the rectal canal from the sigmoid. This may be pathognomonic

TREATMENT

The treatment of sprue is one upon which many views are held.

sprue, and specific treatment is auxiliary It is necessary to point out, *however, that there is a distinct individual and psychological aspect* of the case which must be taken into account in the dietetic treatment of sprue, idiosyncrasy plays an important part, the majority of sprue patients being of the intelligent, impressionable, and introspective type. Some thrive on one dietary. others on a somewhat different one. There are those, for instance, who are partial to and can digest milk products,

s
t

as important as the medicinal treatment, and the patient should look forward to his meals—not resent his dietetic regimen: if he does, it will do him no good.

Every case of sprue must be investigated from all points of view before active treatment is undertaken, and any associated conditions,

body-weight, and the smaller the average size of stool, the greater the increase in weight (Charts 12, 13)

Remarkable increases in body-weight have been recorded by the

becomes more gradual (Figs 68, 69)



Fig 68 —Appearance of patient 24 10.25, before treatment. Weight, 88 lb



Fig 69.—Appearance of same patient 5 1 26, after course of dietetic treatment.

Another point to note is the average weight of the stool in those

It is not necessary to give milk or substitutes alone for more than one week, egg, sago and liver soup may then be added

Mixed diet. [illegible]

irritating protein as the patient is capable of absorbing should be given. The aim is to restore the balance of absorption (Chart 11), and it is with this purpose and from the construction of graphs of this

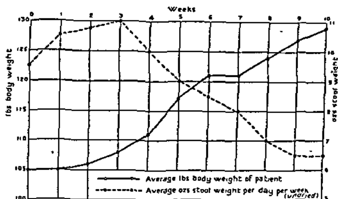


Chart 12.—Graph illustrating that decrease in amount and weight of stool in sprue runs parallel to increase in body-weight. (Average of ten cases.)

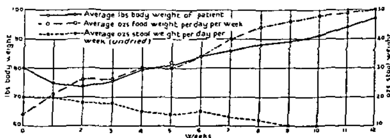


Chart 13.—Graph illustrating the intake of solid matter in the food in sprue and its effect upon the weight of the stools.

nature that the author has designed his treatment of average cases. *Observations on a number of cases have shown that on a mixed milk* and protein diet, with the patient in bed, there is a loss of weight amounting to 5 lb during the first two weeks of treatment, possibly due to elimination of tissue fluids. When once *equilibrium has been* [illegible]

from fresh calves' liver, or from ox liver, and is prepared as follows .—

Three-quarters of a pound of fresh liver is finely minced, and immersed

Eight to sixteen ounces of this soup may be given daily, and to each cupful half a teaspoonful of Marmite may be added. For those who cannot tolerate underdone meat, its appearance and taste may be disguised by adding it to the soup

For those who cannot tolerate it raw, the meat may be slightly cooked in the following fashion .—

toast

A modification is the high-protein dietary (N H Fairley) which has been found suitable for those patients with profound anæmia and signs of intestinal atrophy in whom flatulence and meteorism are pronounced In such cases alimentary rest is the therapeutic ideal, and this can best be obtained by giving the patient a minimum amount of those food constituents which the small intestine fails to deal with

770 in No 1 to over 3,000 in No 5.

Diets for Acute Sprue

Diet No. 1 First Week

(Total calorie value, about 1,000 calories)

Three pints (60 oz.) of cow's milk or Benger's food, in 5-oz. feeds at two-hour intervals; toast, "pulled bread", "Heudebert" rusks; or digestive biscuits with a scrape of butter

Diet No 2 Second Week

(Total calorie value, about 1,900 calories)

Three pints (60 oz) of cow's milk or Benger's food as in No. 1; rusks; toast, sago, 6 oz.; liver soup, 12 oz, in two feeds of 6 oz. each One lightly-boiled egg, weak tea; or sprue tea (i e. tea infused with milk), 8 oz.

Diet No 3 Third Week Onwards

(Total calorie value, about 3,900 calories)

Breakfast.—Porridge, or gruel, 1 egg, toast and weak tea

11 a m.— 10 oz of milk, Sprulac or Benger's food.

Lunch.— Liver soup, 12 oz ; minced chicken, 6 oz, spinach (or cauliflower), 3 oz, sago (or semolina), 6 oz.; baked apple or mashed banana, 6 oz

Tea.— Toast; tea; madeira cake, sponge cake; digestive biscuits (McVitie & Price), 3 oz

Dinner.— Brain or sweetbread, 4 oz ; calves-foot jelly, 3 oz, arrowroot, sago, or tapioca, 8 oz.

Diet No 1 is adjusted to a low calorie value, and while taking it, the patient must be kept in bed and carefully nursed. Diet No 2 is of a higher calorie value; while on this the patient may be allowed to sit up and use the lavatory. During the third, convalescent, diet, he may be allowed up in the afternoon.

[illegible]
onwards and adapted to convalescence according to the special needs of each; it is usually found necessary to persist with this until stools have become normal in size and of average consistency and colour. Convalescent sprue dietary should be nearly 4,000 calories daily, constituted as follows —

Milk, Benger's food, or Sprulac (2 pints)	800 calories
Rusks (10 oz)	750 ,,
Sago (10 oz)	876 ,,
Liver soup (16 oz)	128 ,,
Chicken (6 oz)	390 ,,
Two eggs (4 oz)	180 ,,
Banana (2 oz)	58 ,,
Orange (4 oz)	60 ,,
Extra · Underdone beef (6 oz)	600 ,,

DIET No 5
(Calorie value, 3,020)

6 *a m*—Tea, 10 oz, milk, 2 oz., glucose,* 2 drachms, rusks, 1½ oz, butter, 1 drachm, one scraped ripe apple or one fully ripe Canary banana (yellow ends)

8 *a.m*—Underdone beef, 7 oz, rusks, 3 oz, calves-foot jelly, 2 oz, juice of an orange and glucose, ½ oz, honey, 2 drachms, butter, 1 drachm

10 *a m*—1 baked apple, custard, 3 oz

12 *noon*—Soup, 5 oz + liver extract (equivalent to ¾ lb), underdone beef, 7 oz, calves foot jelly, 2 oz, rusks, 1½ oz; juice of an orange and glucose, ½ oz

4 *p m*—Tea, 10 oz., milk, 2 oz, glucose, 2 drachms, rusks, 3 oz, baked apple, 1 oz, custard, 3 oz (egg, boiled or poached, sometimes substituted), honey, 2 drachms

7 *p m*—The same as at 12 *noon*

Protein fat carbohydrate = 1 0 0 36 2 0

During convalescence a more liberal dietary is permitted, including cauliflower, marrow, celery, asparagus, tomatoes, and fruits Red meats, chicken, and eggs are also advisable, but where carbohydrate intolerance has been a marked feature, small quantities of boiled potatoes and milk puddings are gradually introduced after convalescence has been well established

On this dietary, increase in weight is not so rapid as it is on a diet containing more carbohydrate The objects are to rest the bowel and to afford it a supply of blood which is richer in corpuscles and hæmoglobin When this has been accomplished by the combined liver extract and high-protein dietary, the ratio of carbohydrate is increased in a diet the calorie value of which is sufficient to maintain a steady increase in weight without the return of intestinal distension and gaseous stools

High-protein milk—N H Fairley devised a milk powder which combines the advantages of a high-protein dietary with the bland properties of milk This high-protein milk powder is now manufactured by Cow and Gate, Ltd, as Sprulac It is prepared from fresh milk which is first treated by passage through a gauze and wire filter, is subsequently chilled and centrifuged to get rid of organic and inorganic débris, and is then passed through a mechanical mixing apparatus and desiccated by the roller process at 120° C For use in the tropics it is put up in tins in which the air is replaced by carbon dioxide The chemical analysis of the powder shows —

Moisture	3 0 per cent
Fat	10 6 ,,
Protein	34 0 ,,
Lactose	45 0 ,,
Mineral matter	7 4 ,,

The calorie value per ounce is 125, and the ratio of protein, fat, and carbohydrate is 1 0 0 3 1 3

* Ordinarily 2 drachms of glucose are given twice daily Insulin up to 6 units twice daily can be injected with this diet, and glucose can be increased according to requirements.

Diet No 1

(Calorie value, 770)

8 *a m* —Underdone beef, 3 oz.; juice of half an orange, and glucose, 2 drachms, rusks, ¾ oz *

12 *noon* —Soup, 4 oz + liver extract (equivalent to ⅝ lb.); underdone beef, 3 oz , rusks, ¾ oz , juice of half an orange and glucose, 1 drachm

6 *p m* —The same as at 12 *noon*

Protein fat carbohydrate = 1 0 0 3 1 2

Note —Where patients are very ill, two-hourly feeds of meat and beef juice can be substituted

Diet No 2

(Calorie value, 1,280)

8 *a m* —Underdone beef, 5 oz., rusks, 1 oz , calves-foot jelly, 2 oz.; juice of an orange, and glucose, 2 drachms.

12 *noon* —Soup, 4 oz + liver extract (equivalent to ⅝ lb), underdone beef, 5 oz , rusks, 1 oz , juice of an orange and glucose, 2 drachms.

4 *p.m* —Tea, 10 oz., milk, 2 oz

7 *p m* —The same as at 12 *noon*, with calves-foot jelly, 2 oz.

Protein fat carbohydrate = 1.0: 0.3. 1 0

Diet No 3

(Calorie value, 1,820)

6 *a m* —Tea, 10 oz , milk, 2 oz

8 *a m* —Underdone beef, 6 oz , rusks, 1½ oz., calves-foot jelly, 2 oz ;

[illegible]

uivalent to ⅝ lb), underdone beef

, juice of an orange and glucose, 2 drachms

4 *p m* —Tea, 10 oz., milk, 2 oz ; baked apple, 1 oz , custard, 1 oz.

7 *p m* —The same as at 12 *noon*

Protein fat · carbohydrate = 1 0 . 0 32 : 1 3

Diet No 4

(Calorie value, 2,200)

6 *a m* —Tea, 10 oz , milk, 2 oz

8 *a m* —Underdone beef, 7 oz , rusks, 1½ oz , calves-foot jelly, 2 oz., juice of an orange, and glucose, 2 drachms

10 *a m* —1 baked apple, custard, 2 oz.

12 *noon* —Soup, 5 oz + liver extract (equivalent to ½ lb.), underdone beef, 7 oz , calves-foot jelly, 2 oz , rusks, 3 oz , juice of an orange and glucose, 2 drachms

4 *p m* —Tea, 10 oz , milk, 2 oz , 1 baked apple, custard, 3 oz

7 *p m* —The same as at 12 *noon*, but only 1½ oz. of rusk allowed.

Protein fat · carbohydrate = 1 0: 0 34 1.3

* The best are Heudebert Rusks or the Dutch variety, Verkade's "Groote Beschuit"

have been able to eat a normal diet within six weeks and to resume their normal occupations Four more recent cases can now be cited as

Improvement maintained at least five months without further treatment

pulse and constantly recurring syncopal attacks, tetany and cramps Hæmoglobin 75 per cent, red cell count 2,850,000 In bed 21 days, convalescence delayed by ischio-rectal abscess Treatment with nicotinic acid, 450 mgm daily, plus liver injections—total 54 c c. "campolon" On dis-

necessary

3 —Female, aged 59, three years in Bombay, 1922–1925, 15 years in England before onset of sprue symptoms Seen in October, 1941 Then for 10 months had been suffering from typical sprue symptoms, loss of weight, 64 lbs Flatulence and anæmia pronounced Typical sprue tongue *B coli*

symptoms and feels well

Fruit.—The value of fruit in the treatment of sprue has long been recognized, and in the popular opinion sprue is quite an agreeable disease, which can be treated successfully by a diet of strawberries. Some authorities have held that fresh fruit, or even extracts, exerts an almost specific effect,

To many patients Sprulac is palatable, readily taken, and easily assimilated, and may be made very pleasant by the addition of coffee

The Sprulac diet is made up as follows: One ounce of Sprulac in 8 oz. of water is given every 2½ hours for six feeds a day (7 30 a m to 7 30 p m.), orange juice, calves-foot jelly, baked apples, and custard being gradually added Eventually underdone beef (4 oz.) and rusks are given also.

Milk —In former times the most successful method of treating sprue was by means of the milk cure. This was the treatment adopted by Manson, Van der Burg, Thin, and others. It may occasionally be useful, especially in young adults and the aged

Specific treatment:—Vitamin B_2—Nicotinic acid and riboflavin.—In acute recent cases of sprue, as well as in those of long standing, the author (1941) has recorded outstanding successes with nicotinic acid therapy based upon the principles expressed on p. 356. He has published the end results in a series of 24 cases. It is necessary that patients should be nursed strictly in bed because specific therapy is of little avail until the diarrhœa has ceased.

...ssary to continue with
· three months or even
king testimony of the
ct dietetic precautions
patients in this series

* This is characterized by a flushing of face, an intense feeling of heat, throbbing of the temples and a momentary increase of pulse rate.

mouth-wash twice daily The yellow colour can be effectively removed from the tongue and lips by application of a cloth moistened with a little soap and water

T

ethyl-ester and menthol, and have the effect of anæsthetizing the tongue. Painting the ulcers with equal parts of crystallized carbolic acid and camphor is advocated, and a 1-in-1,000 solution of optochin is also recommended For dysphagia 5 to 10 drops of 1 in-1,000 adrenalin in water every four hours is said to give relief

The treatment of diarrhœa.—The best plan to combat the diarrhœa of sprue is to administer a small quantity of some potent aperient such as castor oil, 2 or 3 drachms, in order to clear out the bowel, after which Batavia powder (Pulv Bataviæ co) checks the diarrhœa This is a modification of the proprietary powder known as "Peter Sys specific," used by Manson, Cantlie, and other early observers The powder is given suspended in milk or water, in doses of 1 teaspoonful (1 drachm) a day, in very obstinate cases of diarrhœa as much as 3 drachms (1 drachm three times daily) is given, but during convalescence it is useful in wafer cachets of 15 grains four times daily Although mythical properties have been ascribed to this powder, equally good results are obtained with Crooke's colloidal kaolin in drachm doses while for nocturnal diarrhœa a bismuth and magnesia mixture (bis oxycarb 15 grains, mag carb pond 15 grains) with chloroform water may be used The author is convinced that, unless the diarrhœa is efficiently checked, no response to specific treatment, as for instance, with nicotinic acid (see p 392) can be attained

Peri-anal irritation or eczema may be very troublesome, and the parts must be kept clean with a diluted solution of potassium

* Made up by B D H

[illegible]

content

The strawberry treatment commences with two or three given with each feed, if found to agree, the number is increased until two or three pounds are taken daily Preserved strawberries and strawberry jam have also been employed, but they do not appear to exert the same effect as does the fresh fruit The author has met with patients who have subsisted entirely, during the height of the season, on a diet of strawberries, and have succeeded in eating as much as 10 to 13 lb of strawberries daily, but usually moderate amounts (½ lb a day) of the fruit fulfil the purpose of a natural laxative. Fresh raspberries and blackberries are almost as well tolerated as strawberries At other seasons of the year, when these fruits are not available, a Canary banana is a welcome adjunct to the diet. Sometimes a dietary of fresh tomatoes is beneficial

Bael fruit (Aegle marmelos) was introduced by Fayrer for the treatment of this disease, and appears to exert a beneficial effect in those countries in which [illegible]

which contains the very potent ferment known as papaine, can be obtained in nearly every tropical country, and is also imported into England,† but unfortunately it does not keep long The pulp is quite agreeable in taste but somewhat insipid; it is easily digestible, and some patients thrive exceedingly well upon it

Other fruits, such as baked apples and stewed plums, are useful Bottled blackberries (especially Southwell's) are of value, and Libby's tinned strawberries and blackberries can also be recommended.

For the constipation that follows the acute stage of sprue, boiled onions, spinach, vegetable marrow, and especially, cauliflower stalks, may be used with great success

MEDICINAL TREATMENT

[illegible]

* The U P. Stores, 15 Lindsay Street, Calcutta

† Lenier and Sherlock, Kingston, Jamaica, and The Army and Navy Stores

such a feature of acute cases, usually responds to injections of vitam B₁ (Benerva Roche), 5 milligrammes daily for five days.

Constipation.—Constipation following the acute phase of

enema of warm olive oil (10 ounces) or even to remove the scyba from the rectum by means of the fingers

abdomen or the immersion of the patient in a bath is often useful

Treatment of tetany and cramps.—Cramps of a group of muscle especially those of the feet and legs, are almost invariable concomitan of a well-marked case of sprue They, and also tetany, which is but more extreme expression, are due to deficient calcium, but when it reduced below 8 mgm. per cent. the administration by the mouth followed by alleviation. The following preparations of calcium a recommended Kalzana, two tablets three times a day, and calciu lactate, 10 grains, three times a day It may be given in a mixture, follows :—

℞ Calc carb	75 gr
Acid lact	200 min.
Aq chlorof ad	8 oz

Mix calc carb præcip with 3 oz of tap water Dilute acid lact wi about 3 oz ... x gradually the two sol Make up to 8 oz wi f this mixture contai

Calcium gluconate (Sandoz) injections (10 c.c.) are also useful extreme cases

... at the end of six weeks

Treatment of sprue anæmia.—In the early stages anæmia respon rapidly to dietetic treatment, and this, when necessary, can be reinforc

permanganate, followed by a dusting-powder of equal parts of talc and boracic acid. The following ointment gives relief:—

℞ Orthoform	40 gr.
Zinc oxide	120 gr
Starch	120 gr
Paraffin ad	1 oz.

three times daily), or a very good preparation known as Charkaolin (Allen and Hanbury).

The following prescriptions are sometimes useful:—

℞ Sp. æther. nitros.	15 min.
Sp ammon aromat.	15 min.
Aq menth pip ad	½ oz.

Occasionally.

℞ Ol. menth. pip	16 min.
Mag. carb.	1 dr.
Cret. prep.	10 gr.
Sod. bicarb.	2 dr.

One teaspoonful in ½ tumblerful of water.

℞ Acid sulph. aromat.	½ oz.
Ol. cajuput.	*40 min.*
Ext hæmatoxyli	3 dr.
Sp chlorof.	1 dr
Syr. zingib	3 oz.

One drachm in ½ tumblerful of water whenever necessary.

Extreme meteorism and abdominal distension.—In advanced cases with atrophy, dilatation of the small and also of the large intestine takes place, so extreme that it resembles Hirschsprung's disease. These cases are very difficult to treat, as the distress caused by the

In extreme cases a rectal tube may be used with success A *glycerin* suppository may also be helpful

Anorexia.—The loss of appetite and distaste for food, which is

such a feature of acute cases, usually responds to injections of vitamin B_1 (Benerva Roche), 5 milligrammes daily for five days

Consti[illegible]

form or in cachets. In extreme cases it may be necessary to give an enema of warm olive oil (10 ounces) or even to remove the scybala from the rectum by means of the fingers [illegible]

Treatment of tetany and cramps.—Cramps of a group of muscles, especially those of the feet and legs, are almost invariable concomitants of a well-marked case of sprue They, and also tetany, which is but a more extreme expression, are due to deficient calcium, but when it is reduced below 8 mgm per cent the administration by the mouth is followed by alleviation The following preparations of calcium are recommended. Kalzana, two tablets three times a day, and calcium lactate, 10 grains, three times a day. It may be given in a mixture, as follows:—

℞ Calc carb	75 gr
Acid lact	200 min
Aq chlorof ad	8 oz.

Mix calc carb præcip with 3 oz of tap water Dilute acid lact with about 2 oz aq chlorof (double strength) Mix gradually the two solutions Stir well until the effervescence ceases Make up to 8 oz with aq chlorof double strength One ounce of this mixture contains approximately 30 gr of calcium lactate

Calcium gluconate (Sandoz) injections (10 c c) are also useful in extreme cases

The realization that sprue is accompanied by a calcium deficiency led H. H. Scott, in 1923, to suggest the routine treatment of this disease by means of calcium and parathyroid He advised that the calcium [illegible]

be continued in full doses until the fifth week, reduced, and stopped altogether at the end of six weeks

Treatment of sprue anæmia.—In the early stages anæmia responds rapidly to dietetic treatment, and this, when necessary, can be reinforced

by iron preparat
accompanied by
as for pernicious
in orange juice, is given immediately after meals, but in the acute stages some cannot tolerate the burning of the tongue and mouth caused by this acid, and hydrochloric acid is then exhibited in the form of tablets of acidol-pepsin or betaine hydrochloride, 2 three times a day.

In extreme anæmia blood-transfusion has been resorted to with success Care should be taken that the blood is carefully matched and that there is no auto-agglutination Large transfusions (above 300 c c) must be avoided, it is probably better to give several small than one large one The author in 1927 published a series of cases in which recovery from extreme anæmia, as well as from all sprue symptoms, took place after a blood-transfusion. The deductions he arrived at from the study of five cases was that the effect was due not so much to mechanical replacement of the destroyed blood-corpuscles, as to stimulation of the blood-forming organs In two instances, more than one blood-transfusion proved necessary to obtain the desired result

Liver therapy—The beneficial effects of liver soup in sprue have already been noted. Since the work of Minot and Murphy in 1926 it has been customary to reinforce this by the administration of liver extracts by the mouth, but this is very expensive treatment, most patients cannot afford it, and it is by no means so efficacious as the

In cases in which there is no satisfactory response to this method treatment, and in cases in which the anæmia is, as occasionally found, of the microcytic type, iron extracts, e g , ferrous sulphate tablets, 5

Additional measures.—In order to promote metabolism and to increase the appetite in recalcitrant cases, small doses of *insulin* have been found useful, commencing with one unit a day and gradually working up to six.

Massage and passive movements are of considerable benefit, especially in men who have been accustomed to hard exercise. They certainly

* *In extreme cases as much as 6 c.c. can be tolerated.*

appear to improve the nutrition of the tissues and promote contentment of mind and body. Massage of the abdomen, however, should be deferred until all the more urgent symptoms have subsided; then, especially in severe constipation, it may prove of considerable value.

Heliotherapy.—Heliotherapy, either by exposure of the patient to the direct rays of the sun or by application of ultra-violet rays to chest and abdomen, has a place in the therapeutics of sprue.

Convalescence

The treatment of convalescence in sprue is an important matter, and, in order to avoid relapses, it is necessary that the patient should reside in an equable climate. Extremes of heat and cold, especially winds accompanied by rain, are likely to produce relapses of diarrhœa. Those people who can afford it are well advised to spend the winter out of England, especially in the Canary Islands or Madeira, where a continuous supply of fresh fruit and particularly tomatoes can be procured. Egypt and North Africa are on the whole unsuitable for sprue patients on account of the extremes of temperature, and also because of the irritating sand and dust. Those who have to remain in England should winter in some mild health resort, such as Torquay or Paignton, or other parts of Devonshire, Cornwall, or the Isle of Wight. The East Coast is particularly unsuitable in the winter and spring months, while sprue patients of Scottish origin should be discouraged from returning to their homeland until the autumn.

For those whose physical condition permits it, walking is by far

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gradually train his body for at least six months before returning to full duties.

A reservoir dose of Campolon (4 c.c.), Pernæmon forte, Anahæmin, or some other liver preparation, given intramuscularly or deep subcutaneously twice weekly, is desirable for several months.

The question of diet in convalescence always arises. The more one sees of this disease the more is one convinced that this is a matter

such as cabbage, broad beans, carrots, and turnips, of potatoes, and of ordinary butcher's meat. Cheese, rich cakes, rich sauces, pastry, and condiments are also definitely contra-indicated. Most forms of

taken before 7.30 p.m. *Any tendency to constipation must be checked* by the addition of more fruit and by taking Petrolagar. Plenty of chicken and fruit should be eaten, and all fatty preparations and starchy puddings avoided. Vegetables such as tomatoes and cauliflower appear to be well tolerated; but such starchy foods as white bread, rice puddings, and beans are not.

CONVALESCENT DIET

Breakfast	
Porridge, made from:	
Quaker Oats	¾ oz.
Milk (or Sprulac)	½ pint
Sugar	¼ oz.
1 Egg, lightly boiled	
Toast	1½ oz.
Tea (very weak)	
11 a.m.	
Warm milk or Sprulac	½ pint
Lunch	
Liver soup	12 oz
Boiled fish	6 oz
Chicken	4 oz.
or Rabbit	4 oz
Spinach	3 oz.
or Veg marrow	3½ oz.
Peas	1½ oz.
or Cauliflower	4 oz.
Milk pudding	½ pint
Baked apple	6 oz
or Banana	3 oz.
Tea	
Toast	3 oz.
Madeira or sponge cake, or biscuits	3 oz
Weak tea	
Dinner	
Brains	4 oz
or Sweetbread	3 oz
Calves-foot jelly	3 oz
Banana	3 oz.
Arrowroot	½ pint

Return to the tropics.—The return of the sprue patient to the tropics is always a vexed question. Unfortunately, the balance of evidence goes to show that when the disease has become well established, even if complete recovery appears to have taken place, on return to the tropics relapse is apt to occur sooner or later. Often the ruling on this point appears to be a very harsh one, as it may mean cutting short the career of young and promising officials. It is difficult to formulate definite rules. The author's own impression, the result of considerable experience, is that the physical and mental state of the patient should be taken as a guide, due regard being paid to his occupa-

tion and age. Those under thirty can be said to recover from sprue completely, and there are numerous instances in which men and women have served for many years in India and the East after suffering from a severe attack It is otherwise in those over fifty, on no account should they be permitted to return if it can be avoided, because in more elderly people, when relapses have taken place, intestinal atrophy

in India and, if careful about their dietary, may remain free from symptoms. The tendency to relapse does not appear to be brought about solely by the tropical climate, because patients who originally contracted their disease in India, may thereafter reside in East and Central Africa with impunity In the author's work on sprue in Ceylon, some twelve cases are cited of people who continued to live on the island for twenty years or more after recovery from sprue

Prognosis.—In the average case prognosis is good, provided that the nature of the disease is adequately recognized and the necessity for strict dieting is appreciated. Since these essentials have become more widely known, and their due value assessed, the writer has found that the hopelessly atrophied cachectics, with capacity for absorption totally destroyed, are no longer encountered The impression gained from older textbooks is that sprue is necessarily a fatal disease, this is, of course, by no means true.

The prognosis depends a great deal upon age The outlook in those below the age of thirty is distinctly good, however bad the symptoms may be, and the patient can be assured of a permanent restoration to health if he continues to live in a temperate climate. The prognosis

the doctor, constitutes half of the battle

It is difficult to state the mortality rate of sprue under modern conditions, but it is somewhere about 7 per cent In elderly people the sprue process may not be the actual determining cause of death. G. Carmichael Low has given the following table in an analysis of his 150 cases

Cured	22
Satisfactory	60
Improved	22
Not improved	16
Died	10
Unaccounted for	20

In the author's series, the mortality rate has been 1 5 per cent.,

excluding those moribund on admission The prognosis has greatly improved since the introduction of Campolon, other liver injections and nicotinic acid.

Prophylaxis.—While the true ætiology of sprue remains obscure, it is very difficult indeed to lay down definite instructions for its prophylaxis, but certain facts emerge and the author feels justified in setting forth his personal views. Undoubtedly, prolonged residence in an endemic zone without regular leave to a temperate climate does predispose to the development of sprue in the European To escape its ravages, regular annual leave to a cooler atmosphere is necessary; a succession of hot weathers in the plain of India must be regarded as a definite factor in causation

such as hot curries, lead to changes in the intestinal tract and to sprue is still unsettled Possibly the frequency with which sprue formerly occurred in veterans, the devotees of club life, was in part due to chronic alcoholism. This led Manson to remark that sprue might be regarded as the past participle of the verb "to spree." There is, however, some evidence that alcohol is to be regarded merely as a

... liable to infection.

...zen or

...ue

HILL DIARRHŒA

... accompanied by flatulent dyspepsia

residing for some time in the hot lowland sof tropical countries, especially India.

History.—A. Grant (1854) originally described hill diarrhœa as occurring at Simla at an elevation of 6,500 to 8,000 feet. It was then considered to be a source of serious inefficiency, and the cause of invaliding among the troops stationed at Simla At first it was

[illegible]

J Duncan, at a later date, put forward the hypothesis that this peculiar form of diarrhœa was due to the presence of mica in drinking-water derived from laterite rocks This hypothesis was subsequently supported by Dyson

Geographical distribution.—It is noted that, in India, at an altitude above 6,000 feet, an atmospheric saturation with water vapour is apparently particularly favourable to the development of hill diarrhœa, outbreaks begin and end with the rains In certain years the disease is apt to assume an epidemic character, thus in 1880, 50–75 per cent of the European population were affected, three-quarters of these within one week In some years hill diarrhœa is less prevalent than in others

According to Pock Steen (1937) a similar affection occurs in the highlands of Java, locally known as "Bandoeng Sprue", it is met with at a more or less definite height on the Preanger plateau. He suggests the possibility of a suprarenal insufficiency, resulting in disturbance of lipoid and carbohydrate metabolism, as explaining the low blood pressure, low blood sugar and increased susceptibility to bacterial toxins Commonly the diarrhœa is a sequel to an acute attack of bacillary dysentery The association of this diarrhœa with allergic manifestations must be borne in mind

Ætiology and pathology.—It is difficult to say what the precise factors are which determine the onset of this disease. The low barometric pressure associated with great elevation above sea-level may be a favouring circumstance, damp seems to be indicated by the fact that the disease occurs principally during the rainy season, while [illegible]

removal from the hot steamy plains to a cool and even chilly station There is an urgent need for further investigation of the physiological consideration here involved, for a complete understanding of the true ætiology may shed light on the genesis of the steatorrhœas

Symptoms.—Without any obvious cause, the patient, who appears

to be in general good health, becomes attacked soon after arrival at

watery in some instances and pasty in others. They are pale and frothy, and have been compared to recently stirred whitewash. The

abeyance for the rest of the day, and the patient may go about his duties feeling perfectly normal. Thus the distinctive features of this

abdomen is blown up like a drum, so that the patient becomes conscious of unpleasant peristaltic movements, associated with a sensation that some chemical process is proceeding inside.

Occasionally cases are met with in which the stools become very pale, although there is no actual diarrhœa; such cases are frequently encountered among passengers on big liners emerging from the tropical heat into the cooler atmosphere of the Mediterranean. It is most necessary that this purely temporary affair should not immediately be regarded as the manifestation of the more serious disease of sprue, although, as has already been pointed out, the one may lead, after a considerable period, to the other. Fock Steen has shown that "pseudo-allergic" symptoms, such as bronchial catarrh and hay fever, may precede the attack but tend to disappear as soon as the sprue-like diarrhœa manifests itself. Urticaria is frequent. Nervous phenomena are also noted, accompanied by low blood pressure and tachycardia

clothed warmly, and given one teaspoonful of liquor hydrargyri perchloridi in water, fifteen minutes after food; two hours later he is

CHAPTER XXII

IDIOPATHIC STEATORRHŒA, CŒLIAC DISEASE, PANCREATOGENOUS STEATORRHŒA

IDIOPATHIC STEATORRHŒA AND CŒLIAC DISEASE

Synonyms.—Cœliac Disease, Gee's Disease, Gee-Herter Disease; Gee-Thaysen Disease, *Die Coeliakie* (German)

History.—In 1888 Samuel Gee published a description of the "Cœliac Affection" in which he gave a clear description of a steatorrhœa occurring in patients of all ages, but especially in young

Intestinal Infection," in which he associated the maintenance of a fair degree of mental development with arrest of the bodily development, marked abdominal distension, and a moderate degree of anæmia He further commented upon the occasional occurrence of rickets, and the changes observed, though rarely, in the tongue, which may be red with swollen papillæ In his biochemical studies, C. A. Herter showed that there is a disturbance of calcium balance, and he further demonstrated that 30–40 per cent of the fat in the stool was in the form of fatty acids This fat loss was not due, he considered, to

It is probable that cœliac disease in children, which manifests itself by digestive disturbances and diarrhœa, is the same as steatorrhœa in adults This aspect has been specially studied by L G. Parsons and A H Miller The pathological changes in the intestinal tract have been studied in Austria by H. Lehndorff and H. Mautner (1937).

The resemblance of this condition to tropical sprue has been com-

mented upon since the time of Gee. In recent years E. H Thaysen has been the chief exponent of this view, which he has summarized, employing a wealth of material, in his book on "*Non-Tropical Sprue*" (1932) He states unequivocally that tropical sprue and idiopathic steatorrhœa are one and the same disease.

The association of tetany with steatorrhœa has been widely commented upon and was specially studied by F. Langmead in 1911. Cœliac disease in children has been found, especially by L. G. Parsons and A. F. Hess, to be the cause of rickets. The hæmatological features of idiopathic steatorrhœa have been studied by G. Fanconi (1928) and E. H. Thaysen (1931).

It has become clear that cœliac disease is not confined to childhood, but may make its first appearance in adolescence or may press itself *on our attention for the first time in adult life, even, it may be, in* old age. It is also to be noted that the disease may be characterized [illegible]

[illegible]

steatorrhœa and osteoporosis developed and the picture became that of cœliac disease It therefore appears possible that this group of diseases can best be explained as an effect of inhibition of phosphorylation through decreased production of adrenal cortical hormone.

Cœliac Disease in Children

[illegible] intestinal indi- [illegible] well-recognized [illegible] study in recent [illegible] cognized as an [illegible] en between one and five years of age; it may, however, remain unrecognized till the child has attained the age of seven or more. Among fifty-four cases analysed the age of onset varied between four months and sixteen years. It is apparently a much more common condition in the British Isles and in Germany than in the United States, L. E. Holt and R. McIntosh state that it occurs only once in every 1,500 admissions to the children's hospital in Baltimore.

Ætiology.—The parents may volunteer the information that the child has exhibited difficulty in digesting milk from the commencement. Both sexes are equally liable to cœliac disease, but heredity appears

to have a definite influence—a matter which certainly requires fuller investigation Fanconi has pointed out that the disease is more frequent in communities where the infant mortality is low

Pathology.—In all cases in which investigations have been carefully conducted no characteristic pathological change has been revealed

No satisfactory explanation of the difficulty in fat absorption is at present available. There is no defect in fat-splitting, and no true steatorrhœa, such as the passage of fat droplets, no changes have been found in the pancreas at autopsy, nor has any evidence of endocrine deficiency been forthcoming H Lehndorff considers that the changes seen at autopsy are consequent upon diarrhœa and malnutrition. The loading of the mesentery with fat has been commented upon

H Thursfield and D Paterson (1934) have suggested that the disorder may be due to some loss of action of bile salts There is a disappearance of glycogen from the liver as the result of chronic disturbance of nutrition Gastric achylia has been found to be the exception rather than the rule The fasting blood-fat is low, but after a fat meal it fails to rise to the normal extent, so that a flat lipæmic curve is obtained There is, therefore, a failure of fat absorption

The fasting blood-sugar may be subnormal, so that a flat low-sugar curve is characteristic The explanation of this curve, as of that in sprue, is still in doubt, but there is good reason to believe that this metabolic defect is similar to that of rickets in small infants It seems that the patient is unable to absorb an adequate amount of vitamin D though a corresponding vitamin-A deficiency has not been noted in cœliac disease E Badenoch and N Morris have shown that the height of the blood-sugar curve after ingestion of glucose increases with

sensitive to the effects of insulin than are normal children

Injection of anterior pituitary extract raises the level of the fasting blood-sugar, and causes a short improvement in the absorption of fat. The radiographical appearances, according to R Golden (1941),

Such children show marked nervous symptoms; they are irritable, extremely difficult to manage, and easily fatigued Development is generally retarded and mentality is slow. In older children, if the disease persists, there is infantilism and retarded sexual development

The gastro-intestinal symptoms are attributable to errors in fat absorption The stools are loose, pale, and copious, but in number

may not exceed one or two daily. In severe cases they assume a frothy and offensive character and the bulk may then be extreme The excess of fatty acids is responsible for the stench of the excreta, and possibly also for the secondary enteritis. Exacerbation of symptoms occurs at irregular intervals and appears to be due to any increase of fat in the dietary

The abdomen is distended, the meteorism being due, mainly, to flatulence. The muscles are flabby and the lower edge of the liver may be palpable In some cases megacolon may develop, especially in those in whom diarrhœa is not severe. The appetite is poor and there is usually a natural inherent reluctance to take fats and milky foods. If the child is forced to eat these, vomiting may occur. Some of these children are so extraordinarily sensitive to fat in food that a small amount may precipitate an attack of fever and diarrhœa.

In severe cases of cœliac disease evidence of interference with the calcium and phosphorus metabolism may appear in defective bone development, e g, in osteoporosis and rickets. The bony changes have been specially studied by L G. Parsons (1933), who regards the rickets as of the late type. Tetany, with Trousseau's and Chvostek's signs, has been noted in these cases. Anæmia may be a secondary [illegible]

ment with iron.

A low degree of nocturnal fever, associated with night sweats and [illegible]

The megacolon developed in infancy may persist in adult life.

Cases in which there is extreme wasting and diarrhœa, and especially those in which tetany develops, are usually fatal The mentality, which is slow, with loss of power of concentration, may improve after [illegible] on a suitable dietary. D. Hunter and others have remarked

European parentage, ranging in age between 2¼ and 7½ years. One hailed from India, one from Hong-Kong, and the third from Malaya In each

the illness apparently commenced as a sequel to an acute attack of dysentery, presumably bacillary The chief features which impressed themselves on [illegible]

Diagnosis [illegible]

due to excessive carbohydrate fermentation

Treatment.—The general principles of treatment are as follows.

1. A low-fat diet, consisting of skimmed milk (commencing with two pints daily), orange juice and green vegetables Later, lean meat, bread, boiled fish, eggs and jam are permitted All fats are to be avoided.

2 Vitamin D is given as irradiated ergosterol (radiostol), with [illegible]

4. For the anæmia, iron and yeast preparations (marmite) are indicated

5. The associated tetany and rickets require special treatment on the usual lines.

Diet.—The essential features of the diet are (1) that it shall contain the minimum of fat, and (2) that the protein and carbohydrates shall be in a form acceptable to the child's digestive capacities

[illegible] diet. For

may not exceed one or two daily. In severe cases they assume a frothy and offensive character and the bulk may then be extreme The excess of fatty acids is responsible for the stench of the excreta, and possibly also for the secondary enteritis Exacerbation of symptoms occurs at irregular intervals and appears to be due to any increase of fat in the dietary.

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In severe cases of cœliac disease evidence of interference with the calcium and phosphorus metabolism may appear in defective bone development, e.g., in osteoporosis and rickets. The bony changes have been specially studied by L. G. Parsons (1933), who regards the rickets as of the late type Tetany, with Trousseau's and Chvostek's signs, has been noted in these cases. Anæmia may be a secondary factor, and appears to follow the same lines as in steatorrhœa of adults; that is, it may be simple hypochromic anæmia responding to iron, or a megalocytic hyperchromic anæmia responding to liver or to yeast (marmite) therapy. On rare occasions there is a type resembling "Cooley's" anæmia—an erythroblastæmia, which responds to treatment with iron.

A low degree of nocturnal fever, associated with night sweats and persisting for months, is common; less frequently, bouts of high fever may occur, preceded by loss of appetite, coated tongue, and sallowness.

[illegible]

The megacolon developed in infancy may persist in adult life.

Cases in which there is extreme wasting and diarrhœa, and especially those in which tetany develops, are usually fatal. The mentality, which is slow, with loss of power of concentration, may improve after puberty and on a suitable dietary. D. Hunter and others have remarked that children with chronic cœliac disease may develop signs of pellagra

The writer has encountered three cases of cœliac disease in small boys of European parentage, ranging in age between 2½ and 7½ years. One hailed from India, one from Hong-Kong, and the third from Malaya. In each

E H Thaysen described various degrees of glossitis in the majority of his "non-tropical sprue" cases.

Gastric analysis revealed complete achlorhydria with no total acidity in only two out of twelve cases examined Abdominal distension was a conspicuous feature in some cases, but was not present in every instance Where there is extreme meteorism there may be some difficulty in differentiating the disease from tuberculous peritonitis In six out of eight cases a marked dilatation of the colon was detected by X-ray examination, and in two it was pronounced enough to be designated megacolon There appears to be a definite relationship between the diarrhœa and dilatation of the colon—the greater the

diarrhœa, steatorrhœa was present in every case The total fat varied from 47–71 per cent of all the stools analysed Tetany was present in fourteen cases and skin lesions in seven, usually in the form of an

comments upon the diminished height and the laborious, cautious gait, comparable to the hunger osteomalacia seen during the 1914–18 War In Bennett and Hunter's series no normal skeleton was encountered Ten cases were dwarfed, but the infantilism of stature was not necessarily associated with mental or sexual infantilism In twelve cases, whether dwarfism was present or not, the bones were in some way deformed Osteoporosis of varying degrees was seen in twelve cases It has been noted, however, that there may be no physical signs of associated hypocalcæmia even with a low blood-calcium content

The blood-picture was normal, or showed a hypochromic anæmia,

thirteen cases the serum-calcium was low

Irregular attacks of pyrexia have been noted, associated especially with intestinal disturbances.

of carbohydrates, but the form in which this is best tolerated varies greatly with the individual child. Dried cereals (Post-Toasties, Cornflakes, Force, etc.) are useful, and may be served as puddings, made with skimmed dried milk. Ripe bananas are widely used, and chestnut flour is a useful variant.

[illegible]

aged four years :—

Separated Cow & Gate (1 drachm with water to 1 ounce)	20 oz.
Dextrin	1 oz.
Plasmon biscuits	*4 oz.*
Powdered casein	3 oz.
Cheese	3 teaspoonfuls
Butter	1 teaspoonful
Honey	1 teaspoonful
Post-Toasties	*5 tablespoonfuls*
Chestnut flour as pudding	2 tablespoonfuls
Radiostoleum	3 minims t d s

Egg and small quantities of cow's milk are gradually introduced. Later green vegetables, potatoes and carrots are added.

IDIOPATHIC STEATORRHŒA OF ADULTS

Cœliac disease in adults has only comparatively recently been recognized, and the history of its discovery has already been alluded to There are many reasons, detailed on p. 377, for its differentiation from *tropical sprue, though many of the clinical and biochemical features* are similar Interest has been aroused by the frequency of this affection in Denmark and other parts of northern Europe, and there is every reason to believe that many instances of non-tropical sprue, so ably described by Thaysen, are identical with idiopathic steatorrhœa of adults which has been recognized in England. E. J. Wood first described this condition in the United States, where it was first thought to be tropical sprue

[illegible] can be traced [illegible]

same symptoms are present as are seen in cœliac disease in children—dilatation of the colon, tetany, osteomalacia, anæmia, infantilism, steatorrhœa, disturbance of calcium metabolism expressing itself in skeletal changes, osteoporosis, and often rickets. Glossitis occurred in five cases The patients may not actually complain of sore tongue, but the tongue presents the bald and shiny appearance, due to atrophy of the filiform papillæ, so frequently associated with anæmia. In contrast to the almost constant occurrence of sore tongue in tropical sprue, this symptom is only occasional, though it must be noted that

hydria

The case was observed in hospital for three months before death. Blood-transfusions, injections of calcium gluconate and parathormone (Collip), all kinds of diet, etc, were tried, but no treatment had any effect in stemming the downhill progress At autopsy the liver, heart and spleen were found to be small and atrophied The intestinal walls were thinned and transparent, the bones soft and pliable No other important features were noted

regarded as somewhat problematical, and how far they are applicable to tropical sprue is yet uncertain.

R Golden (1941), and I J Mackie in America, while the first-named has claimed that they are modified by adequate liver therapy.

It is stated that the changes in the small intestine are the result of intestinal hurry and interference with normal mixing of intestinal

Treatment.—The treatment of steatorrhœa in adults follows the same lines as that adopted for children, the chief points being control of the steatorrhœa by a low-fat diet, control of the carbohydrate dyspepsia by regulation of the intake of starch, relief of tetany by increasing the intake of calcium and of vitamin D, alleviation of the pain and relief of bone deformities, and finally the treatment of the anæmia by increasing the intake of iron, or by giving marmite or liver

H. Moore, W. R. O'Farrell, J. A. Geraghty, J. M. Hayden and M. A.

present in every case, and multiple fractures were present in three; in one there were five fractures, in one seven, and in another nine. Under treatment they all united.

R. Kark, A. W. Souter and J. C. Hayward (1941) have made the

suffered from recurrent ecchymoses over the backs of hands, elbows, knees and scapular area.

Diagnosis.—Diagnosis is made upon the indications which have already been given. There appears to be no essential point of distinction between the features described by Thaysen and those so ably put forward by T. I. Bennett, D. Hunter, and J. Vaughan.

Reference must be made to the condition known as "congenital steatorrhœa" which is characterized by the passage of butter-like stools, and has been included by Garrod amongst the inborn errors of metabolism. Cases have been described by R. Miller and H. Perkins (1923) and Spriggs and Leigh during recent years. It is not associated with infantilism or bony changes, and therefore has no relationship to idiopathic steatorrhœa.

The differential diagnosis has to be made from sprue and other

In the first place the tongue and

illustrated by a case seen by the author :—

A man of fifty-one years of age was referred from Dumfries-shire with the provisional diagnosis of sprue on February 25, 1937. He had never been but had served in Salonica from 1915 to 1917. He had been

PANCREATOGENOUS STEATORRHŒA

Pancreatic Insufficiency —The normal pancreatic juice contains trypsinogen, the zymogen of trypsin (protein ferment), lipase or steapsin (fat ferment); and diastase or amylopsin (starch ferment).

The considerations upon which a diagnosis of pancreatic insufficiency may be based are as follows —

1 **Internal secretion.**—The efficiency of the internal secretion is tested by means of Loewe's adrenalin mydriatic reaction, which consists of placing two drops of 1 . 1,000-adrenalin solution on the conjuctiva, and repeating in 15 minutes If the pupil dilates, it suggests a deficiency of the pancreatic secretion

2 **External secretion.**—The most definite results of failure of this secretion are (1) steatorrhœa (excessive excretion of fat), (2) azotorrhœa, (excessive excretion of protein), and (3) increase of diastase in the urine

Steatorrhœa, or "pancreatic stools," results from a deficiency of pancreatic ferments The stools are bulky, frothy and light-coloured, with an offensive "cheesy" odour mainly due to excess of fat The chemical alterations in the stools are mainly due to the excess of fat, which amounts to 50–80 per cent of the total weight, and consists mainly of neutral fat, which cannot be absorbed The reaction of the stools is alkaline Comparison should be made with stools of sprue, cœliac disease, and idiopathic steatorrhœa, which are acid and the excess of fat is due to fatty acids and soaps

If the pancreatic secretion is defective, the stools show a large amount of undigested fat, represented by an abnormal percentage of neutral fat, on the other hand, if bile is deficient, the large amount of undigested food is composed of an abnormal percentage of split fat

Azotorrhœa —The amount of protein recoverable from the stools in pancreatic disease is 30 to 40 per cent, whereas from normal fæces it is about 5 per cent

[illegible]

form appears to be the result of irregular necrosis and autolysis *Pancreatic calculi* are of little practical importance, except when impaction occurs with either acute necrosis or sclerosis of the pancreatic tissues

Acute necrosis of the pancreas.—This is due to impaction of a gall-stone or pancreatic stone in the ampulla of Vater, or it may

Patients can seldom be given as much fat as is present in normal diet without suff[illegible] should in all cas[illegible] lactate in doses [illegible] injections of cal[illegible] should be given in every case in which there are clinical or radiographic signs of rickets, osteomalacia, or osteoporosis. It often relieves the bone pains, but any relapse of diarrhœa is apt to interfere with its good effects It is best given in the form of radiostol tablets (B.D.H) In



Fig. 70.—Idiopathic steatorrhœa : facies and tongue of the case described in the text.

treating all the forms of anæmia, it is necessary to remember the importance of adequate dosage. Injections of Campolon or Hepatex should be given in 6 c c doses daily. Iron and marmite should be given according to the type of anæmia present

[illegible]



Fig 71 —Tropical sprue in acute stage, to show fat globules and fatty-acid crystals.



Fig 72 —Pancreatitis, showing fatty-acid crystals, fat globules and undigested starch granules.

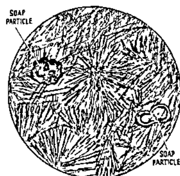


Fig 73 —Biliary cirrhosis, showing sheaves of large fatty acid crystals.

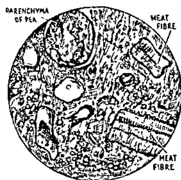


Fig 74 —Fatty fæces of biliary obstruction, showing undigested meat-fibre

Figs.—71–74 —Microscopic appearances of the fæces in the steatorrhœas.

[illegible] gurgitation of bile [illegible] s thus prevented, [illegible] escape of lipase [illegible] tissues.

[illegible] these individuals [illegible] ually arises as a sequel of infections such as influenza, typhoid, or mumps A history of gall-stones is frequently obtained. In alcoholic subjects, who are liable to attacks of gastro-duodenitis, the inflammation may spread to the pancreas through the pancreatic ducts.

The most obvious symptom is progressive wasting with intense indigestion. As a rule, gastro-intestinal symptoms are indefinite and various. Everything from vague slight distress to severe indigestion with nausea is encountered. Either diarrhœa or constipation may manifest itself There is usually severe and agonizing epigastric pain, which is thought to be due to irritation of the cœliac plexus.

Chronic pancreatitis.—Chronic pancreatitis may arise from inflammation within the ducts and may be due to pancreatic calculi, to gall-stones in the ampulla, or to spread to the pancreas of inflammation of the bile-ducts caused by gall-stones A history of biliary colic and gall-stones is present in 50 per cent. of cases. The symptoms are usually indefinite, and consist of recurrent attacks of pain in the epigastrium, rigors, fever, sweats, vomiting, and diarrhœa, very often accompanied by bulky pale stools. The symptoms may simulate gall-stones, so that jaundice is a frequent accompaniment. Glycosuria and diabetic symptoms are rare

Stools.—The peculiar pale bulky motions encountered in chronic pancreatitis are especially noticeable when the gall-bladder is involved It is important to note that much of the unsplit fat, to which reference has already been made, is decomposed by the action of intestinal bacteria in the lower part of the gut. Special attention should be directed towards the microscopical appearances (Figs. 71–74).

In **carcinoma of the pancreas** the pain is exceptionally severe, [illegible]

Affections of the Colon Resembling Dysentery

CHAPTER XXIII

MUCOUS COLITIS

Synonyms.—Muco-membranous Colitis, Membranous Colitis, Irritable Colon, Spastic Colitis; Mucous Colopathy.

Definition.—The term "mucous colitis" is a convenient one [illegible]

[illegible] the cause or the result of the disease Mucus is a glycoprotein, a normal secretion both of the stomach and of the intestine, and is able to take up large quantities of water and dissolved substances The normal mucus fulfils the functions of softener, lubricant, and protective, and its production is much increased in infective processes W N Boldyreff suggests that excess of mucus is harmful to the digestion A F Hurst considers that the mucus in the stool has been secreted as a response to irritation caused, for instance, by the fæces which, when they collect in the pelvic colon, are often hard and dry

Ætiology.—A great deal has been written upon the genesis and treatment of this affection [illegible] ha[illegible] a [illegible] ne[illegible] col[illegible] often employed, implies that the musculo-neural apparatus has lost its powers of co-ordination and correlation, probably the fact is that this condition actually precedes the development of mucous colitis The excessive secretion of mucus is usually associated with spastic contraction of the colon or "spastic colon."

W A. Bastedo and others who have written about this malady agree "that there is much difference of opinion about its character and no agreement about its ætiology"

The following theories have been put forward · 1 That the condition is purely neurogenic and that the mucus produced in the bowel is a hypersecretion; 2 That the condition is catarrhal, the result of inflammation of the mucous membrane of the colon; 3 That the condition is in part neurogenic and in part inflammatory, 4 That the condition is in part, or wholly, due to hypersensitivity to the normal bacterial inhabitants of the intestinal canal, 5. That it is an intestinal manifestation of an allergic disease

essential rôle of the nervous system in governing both the motor functions of the bowel and its secretion of mucus. It is not easy to determine whether abnormalities of mucus secretion and of bowel action cause the symptoms, or whether symptoms and abnormalities of mucus secretion are alike the result of disorder elsewhere in the body. F H Kruse has devoted attention to the innervation of the intestinal tract in his search for an explanation of spastic colitis, and he considers that the parasympathetic nervous system, notably the vagus, is the activator, while the sympathetic system with its paravertebral ganglia acts as the inhibitor or depressor Auerbach's plexus, on the other hand, is chiefly concerned with the act of peristalsis, and the sacral plexus with the muscular tonus of the bowel.

E I Spriggs, in a scholarly and penetrating analysis of mucous colitis, gives it as his opinion that the two main causes are neurosis and constipation His experience leads to the view that an unstable nervous system is a predisposing factor. The pronounced form of the condition known as enterospasm is usually found only in those engaged in mental work The almost constant complaint is constipation, and in his opinion the treatment of real or alleged constipation by irritating aperients is as potent and frequent a cause of colonic disorder as is the constipation itself He holds, indeed, that constipation is less harmful to the colon than are the irritative aperients

C Hunter (1932) considers that the peristaltic action of the colon is normally and automatically regulated by impulses from Auerbach's

inferred from a case reported by W A Bastedo in which the colon was removed, yet all the symptoms of mucous colitis, even to colic and

common
nature
Bargen,
In 50
cases, J. A. Ryle found 17 males and 33 females, the age limits being nineteen and seventy-eight years A similar condition is recognized in infants and children

The type of person who develops mucous colitis has often been

Occupation appears to have a definite bearing on the incidence.

The allergic factor.—Allergy is defined as a condition of altered

Familiar

fever,

of the

al and

circular muscle fibres takes place Various authorities have reported

foreign proteins Mechanical factors must also be taken into consideration, as the mucous membrane of the bowel is very irritable when the bowel is in a sensitive state. (A. A. Bissett.)

between the first onset of colitis and such infections of the upper respiratory tract as influenza, acute catarrh, and tonsillitis The allergic respones of sensitized tissues is characterized by increased permeability of the capillaries, œdema of the mucous membranes, and spasm of unstriped muscles, it may be limited to the colon. It is pointed out that one of the functions of the colon is excretion, and it may be that *bacterial products expose the tissues to special damage* or sensitization

food, and daily bowel evacuations. It is the mode of life of the

that pro-

the vicious

what is

upon the

be so dense as to resemble actual mucosa, when it is often mistaken for a membrane.

The fæces may be characteristic of the different types of the disease. Where the colon is very irritable there are scybala surrounded by mucus. In catarrhal mucous colitis the mucus is very much increased

usually bleeding both before and after passage of this membrane

Sometimes the mucus is passed intermittently, when the stools come to resemble some badly-made meat jelly or under-cooked vegetable marrow The amount of mucus passed per day is very variable —it is said that as much as 1,000 c c may escape. In colour it is grey, greyish-white, or brown. The passage of mucus in the stools is very disturbing to most patients, but this is due not so much to any associated distressing symptoms, but rather to the fact that the patient's attention has been directed to the presence of this abnormality.

morphia

periods of

taking of f

much rumb

the patient's attention to his stomach as the cause of his intestinal disorder

must be d

fusing the

Ryle in E

that a spastic colon is a common cause of persisting and recurring pain in the right iliac fossa, and that it may, therefore, closely simulate appendicitis

There are also various nervous disorders associated with this condition—nervous exhaustion, mental depression, lack of concentration, persistent headache, paræsthesia, syncope, and vertigo. Dead and

usually be palpated and is tender on deep pressure, especially in the left iliac fossa. Occasionally, the ascending and transverse colons may be felt as a hard cord

ity

ex

fact it may be said to be as common among the busy public servants in hot countries as it is among business people (especially those of

canal.

Investigation into the previous histories of genuine cases of mucous colitis in the tropics has shown that, when a person of a certain type of mentality has suffered from some form of dysentery, his mind, having become concentrated upon the functions of his intestines, exerts an undue influence over the bowel, and sooner or later mucous colitis develops. The danger of not recognizing the true nature of such cases can readily be appreciated, because consistent treatment for well-established dysentery only exacerbates the bowel condition.

Definite hyperthyroidism, 2.	Dental sepsis, 3.
Hyperchlorhydria, 2.	Giardiasis, 1.
Chronic appendicitis, 2.	Syphilis (W R ++), 2.
Internal hæmorrhoids, 2.	*Diverticulitis*, 1.
Trichuris trichiura infection, 1.	Urticaria, 1.
Ascaris infection, 1	Septic tonsillitis, 1.
Gall-stones, 1.	

Symptoms.—Although the symptoms of mucous colitis resemble

the fæcal masses are of small calibre, and flattened or ribbon-like.

period.

Mucus is present in the stools in variable quantities at different stages of the illness. When the patient is badly constipated, efforts at passing a motion may result in the outpouring of several ounces of gelatinous mucus, which is often passed in ropes or strings, and may



Photo Dr G Mather Cordiner

Radiograph of liver, showing gas in liver-abscess cavity after aspiration (*Dr N H Fairley's case*)

AMŒBIC ABSCESS OF LIVER

PLATE XIII

Smith, Paul, and Fowler found that the experimental introduction of 500 c.c. of air into the colon by means of a rubber bulb and rectal tube was followed at once by a striking increase in tone of the pyloric end of the stomach

In its most intense form this colitis is accompanied by the passage of membrane and casts of the large intestine, and is then by some authorities designated as membranous colitis. Since, however, in these cases accumulations of mucus, which closely simulate a membranous cast, are quite commonly extruded from time to time, the term *muco-membranous colitis* is more accurate. Such severe cases are by no means common, and when they do occur are distinctly more distressing and more difficult to treat than are cases of the ordinary mucous colitis.

There are few descriptions of this muco-membranous colitis in the literature. The patients are usually young adults, the majority being women, and are of a highly sensitive, introspective type. From time to time they suffer from attacks of severe intestinal pain and colicky spasm, accompanied by the passage of a cast of the mucous membrane of the large intestine; usually this is only a few inches in length, but

Trichuris

On several occasions when in hospital she was attacked by bouts of



Radiograph of barium enema in mucous colitis, showing characteristic spasm of descending colon and sigmoid.

MUCOUS COLITIS

PLATE XIV

very often hæmolytic streptococci also, but they appear to be of no diagnostic significance.

introduction of the instrument causes a reflex contraction of the bowel. On account of this spasm, considerable difficulty may be experienced in

and hypochondriasis

In many cases the pain experienced is of that degree of severity to be expected in acute inflammatory conditions of the bowel, in others, though of course it may be less severe, it is none the less chronic. It is, therefore, hardly to be wondered at that the patient's mind dwells with anxiety upon the significance of the symptoms. J. A. Ryle has pointed out that most of these patients live in constant dread of some severe organic disease of the intestines.

Treatment.—The treatment of mucous colitis and spastic colon is by no means easy. It should be so planned as to minimize the fears the patient entertains regarding himself, and to foster a sense of confidence in the ability of his medical attendant to cure him. The first thing to do is to try the effect of a psychotherapeutic approach—to convince him that, however serious the signs and symptoms may appear, they are not an indication of a severe or incurable malady. Indeed, the mortality from muco-membranous colitis may be set down as nil.

Great care should be taken regarding the previous history of the [illegible]

that mucous colitis should never be diagnosed from X-ray findings alone. (Plate XIV.)

Examination of fæces.—The stools may consist of hard scybalous masses coated with whitish strings of mucus, or they may be semi-formed and gelatinous owing to the liberal admixture of mucus derived from the bowel wall. Where there has been exfoliation of the mucosa, as in muco-membranous colitis, a cast of the mucous membrane of the whole tube or of small portions of it is recognizable. It is necessary to emphasize that this membrane is not passed with every motion, but only during the periodic exacerbations which occur in this form

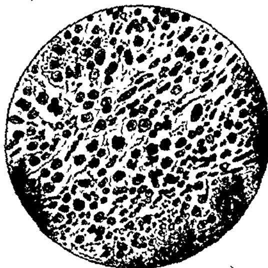


Fig. 75.—Appearance of mucus-secreting cells in the exudate in mucous colitis.

The author believes that considerable help may be obtained from a microscopic examination of the fæces. The cellular exudate in mucous colitis consists mainly of mucous cells and remains of goblet cells, which may be recognized amidst the glairy mucus. (Fig. 75) Very often columnar intestinal cells are also visible, as well as squamous cells derived from the anal margin. A. F. Hurst has emphasized that *the mucus never contains leucocytes or red blood-corpuscles*

Intestinal sand was found by W. Hale-White in 10 per cent. of his cases. It occurs intermittently, and as much as a tablespoonful may be passed in a day. It consists mostly of calcium phosphate with traces of oxalate, and of magnesium, iron and silica.

Bacteriological culture of the fæces is distinctly misleading A variety of intestinal coliform organisms can usually be isolated, and

10 ounces of olive oil and used as a retention enema, has also been found to be of great benefit. Cod-liver oil emulsion—in the proportion of 1 part to 4 parts of water (as retention enema)—is agreeable and very soothing Eight ounces should be injected

As emphasized by Bargen, *occupational therapy* plays a great part in the treatment of this colitis A patient must try to cultivate a suitable frame of mind in order to get the best out of his treatment,

the treatment of mucous colitis, so that authorities differ greatly in their opinions on this subject The diet should be generous, varied, and well-balanced free from irritating ingredients such as tough meat and vegetable fibres Milk in large quantities does not usually agree Eggs in scrambled form, in omelettes, or in custard, with junket, plain and cream soups and well-cooked milk puddings are permitted

Fish and meat—Fish is to be recommended—boiled, steamed, or baked, but not fried, also chicken or game, whether roast or baked, tripe, well-

be allowed

Drinks—Mucous colitis patients should drink sparingly at meals, but plenty of water should be drunk between them Freshly-made weak tea, or coffee with milk, and light wine, are best

Food should be taken regularly Frequent small feeds are recommended

The treatment of mucous colitis in children—Children with acute mucous colitis should be given no solid food All milk should be stopped, and glucose water or orange juice and water substituted. When the desire for food has returned, one of the dried milks, such as skimmed Cow and Gate, Glaxo, or Horlick's, should be commenced. As stools improve, the child should be encouraged to take more solid diet, such as junket, custard, milk puddings, etc.

Medicines are not of great value for children Bismuth oxycarbonate and Kaylene in large doses, ½–1 drachm, should be given three to four times daily, and the following is a very useful mixture —

℞ Pulv rhei	2 gr
Pulv jalap	2 gr
Pulv scammon.	2 gr

To be given three times daily

Prognosis.—In the minor forms of mucous colitis, the outlook is good if the underlying cause of the malady can be dealt with If it

This calls for lubricants, such as liquid paraffin (1-2 drachms), or Petrolagar. Whether constipation is actually a fact can be established by a barium meal.

Treatment to re-establish the function of the colon.—For the pain of colonic spasm, there is nothing more useful than a mixture of bromide and belladonna such as the following.—

℞ Tinct. bellad	5 min
Sod brom	5 gr.
Aq chlorof. ad	½ oz.

Half an ounce to be taken morning and evening.

The addition of tincture of hyoscyamus to this mixture may be of distinct value.

Stacey Wilson and others have advocated the following mixtures.—

℞ Liq ferr perchlor.	15 min.
Liq hydrarg. perchlor	15 min
Tinct. hyoscy.	15 min
Syr. aurant	60 min
Aq chlorof. ad	½ oz

Half an ounce with water three times daily, ten minutes before meals

℞ Bism. salicyl	15 gr.
Salol	10 gr.

To be made into a powder.

or ℞ Bism. salicyl.	5 gr
Salol	5 gr
Calomel	¼ gr.

In tablet form. To be taken three times daily before food with a small quantity of water.

For acute attacks of colonic spasm, there is nothing so efficacious as full doses of atropine sulphate (1/50–1/100 grain) given by injection, and sometimes adrenalin 1 : 1,000 (5–10 minims) by hypodermic injection is useful

For soothing the bowel, the author has found Iso-gel (Allen and Hanburys) in large doses very good relief to the patient's general comfort.

times daily,
(Petrolagar
gation of the
quantities of
the secretion

of mucus by unnecessarily irritating the mucosa J. G Mateer and J I Baltz recommend sodium ricinoleate, in 5-grain enteric-coated "soricin" tablets, three times daily *before* meals, given over a long period. The routine dose should be six tablets a day. Moderate injections of a bland substance, such as warmed olive oil (5–10 ounces injected slowly) act as a soothing agent and a mild aperient. The routine treatment with bismuth subgallate, 5 per cent suspended in

10 ounces of olive oil and used as a retention enema, has also been found to be of great benefit. Cod-liver oil emulsion—in the proportion of 1 part to 4 parts of water (as retention enema)—is agreeable and very soothing Eight ounces should be injected

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To be given three times daily

Prognosis—In the minor forms of mucous colitis, the outlook is good if the underlying cause of the malady can be dealt with. If it

is constipation, or the unregulated use of aperients, then the remedy is easy. The neurasthenic symptoms may also be mitigated when the patient has succeeded in regaining confidence in himself Those cases with colospasm or painful spastic colitis do very well after a prolonged holiday and relief from mental strain. It must be remembered both by the patient and his medical adviser that the condition is not inherently serious, and is never fatal. At its worst it is an inconvenience

Prognosis is naturally better when the case is taken in hand early, and is seriously and energetically treated. The subject of intestinal neurasthenia with recurrent membranous crises is a particularly difficult patient to deal with. But no cases are so hopeless that all attempts at further treatment can be discarded. However tragic these crises may appear, they do not in any way tend to shorten life.

CHAPTER XXIV

IDIOPATHIC ULCERATIVE COLITIS

Synonyms.—Colitis Gravis (German), Chronic Ulcerative Colitis, Thrombo-Ulcerative Colitis, Ulcerative Recto-Colitis, Granular Rectitis.

Definition.—The term "colitis gravis" is in many ways preferable to "ulcerative colitis" as it embodies the main features of this severe disease. The latter is by no means a satisfactory designation, because ulceration of the colon is not invariably present, and, when it is, it usually denotes a fatal termination. The tendency to acute inflammatory exacerbations and to periods of quiescence abruptly terminated by relapses, would entitle it to the designation "non-specific inflammatory colitis". Nevertheless, the term "ulcerative colitis" has been so hallowed by long usage that it has attained an international character and is therefore retained. There remains, however, no doubt in the minds of those who have studied the subject that, whatever it is called, it represents a distinct disease

tion it in their lectures on pathological anatomy. Allchin, in 1885, exhibited a typical colon at the Medical Society of London and in 1888 W. Hale-White described the condition well. P. Lockhart-

bacillus at the autopsy on a child in Great Ormond Street Hospital, London, and since then he has found that this bacillus is responsible

for cases of chronic colitis in small children. It is not, however, by any means proved that these cases correspond to cases of ulcerative colitis in adults. Recently A. F. Hurst and F. A. Knott have returned

workers consider that ulcerative colitis is a direct sequel of a previous dysenteric infection of which the organisms and the agglutinins they evoked in the blood have disappeared.

D Kling has consistently regarded ulcerative colitis as being of

further examined the stools for the presence of anti-dysentery bacteriophage, and claim that they were able to demonstrate such an active substance in 36 per cent. Intradermal tests with dysentery toxins gave approximately the same percentage as did normal controls.

T. T. Mackie (1932) considers that the lesions of chronic bacillary dysentery differ in no material respect from those encountered in many cases of ulcerative colitis, and he confirmed this by isolating

find any previous dysenteric infection.

Mucous colitis theory—There are many who think that ulcerative

—who have, for instance, rectal disease. In one-half of his cases rectal disease had preceded the ulcerative colitis, but then, in half it had not.

reiterated
his the fæces
an ated from
peri-apical dental abscesses in 140 patients with chronic ulcerative colitis and has also been found in the tonsils of 100 ulcerative colitis patients. T. J. Cook obtained cultures of the diplostreptococcus from



1, Acute hæmorrhagic colitis, 24 hours after prostatectomy, resembling acute bacillary dysentery. (*From London Hospital*)



2, Acute ulcerative colitis of ascending colon. (*From Hospital for Tropical Diseases*)



3, Subacute ulcerative colitis of sigmoid colon, showing great induration (*From Hospital for Tropical Diseases*)



4, Chronic ulcerative colitis with gross destruction of mucosa (*From Hospital for Tropical Diseases*)

PATHOLOGY OF ULCERATIVE COLITIS

PLATE XV



Photo Dr G Mather Cordiner

Radiograph of large intestine (negative), demonstrating regional ulcerative colitis affecting transverse and descending colons. (*Dr N H Fairley's case*)

ULCERATIVE COLITIS

PLATE XVI

from approximately 80 per cent. of patients with chronic ulcerative colitis who were examined at the Mayo Clinic over a period of several years Belief in the specificity of this organism is strengthened by the fact that frequently tonsillectomy, removal of infected teeth, or acute infections of the upper respiratory tract cause marked exacerbations

and preparations were made and stained for diplococci Eventually the diplococcus was isolated in blood agar and found to ferment dextrose, lactose, saccharose, maltose, raffinose, and salicin

These facts have convinced Bargen and his collaborators that chronic ulcerative colitis is a disease of bacterial origin and that the primary exciting factor is the diplostreptococcus Their results have been confirmed (1934) by H. H de Jong, and others

G M Dack, T. E Heinz, and L E Dragstedt (1935) made a bacteriological

Rodaniche *et al* (1940) have repeated Paulson's work and have concluded that *these two diseases are quite separate in their ætiology.* The confusion has probably arisen from the somewhat similar symptoms evoked in early cases of

vitamin A and the vitamin B complex are necessary for the development of a healthy mucous membrane in the intestine and for maintaining resistance to infection.

Ulcerative colitis resembles the deficiency state in so far as it occurs in attacks

concerned with the excretion of calcium, iron, and bismuth The special tendency of metabolic toxins to cause colitis, as in uræmia, is probably due to their elimination by this route.

T T. Mackie and R E Pound (1935) claim to have demonstrated a

also involved.

Predisposing factors —In this connexion T. A Bargen and J. W. Kemble (1935) specially investigated twenty patients In no instance was another member of the same family affected; nor did the previous history of the sufferer yield any positive information The psychical element as a pre-

in this disease.

A. H Logan published a statistical study of 117 cases, which is the largest series reported up to date He believes that the basic factor is some metabolic disturbance.

held concerning the

excretion of toxins through the intestinal mucosa, resembling in this

rhagic colitis
ed by J. A.
ie pathology
patients of a

Pathology.—According to most authorities, including C. Dukes, ulcerative colitis begins as an acute inflammation of the mucous

membrane of the colon; this leads to necrosis, which may be partial or widespread, and is followed by the separation of sloughs and by superficial ulceration. Should the ulcers heal up, ragged polypoid

destruction, there are islands of mucous membrane in the descending and iliac colons which appear to have escaped almost entirely (Plate XV, 2-4)

pathology derived from post-mortem examinations appears to be

may commence anywhere in the large intestine, sometimes even in the cæcum, and the pathological picture is the same whatever portion of the bowel is involved

Thickening of the bowel-wall is almost invariable In the acute

Injury to the nerve supply of the bowel (notably in Auerbach's plexus) undoubtedly results from such extensive inflammatory changes,

dysentery.

S. Lups (1935), and others have called attention to shrinkage and shortening of the large intestine This occurs particularly in the descending colon, but in a few cases the cæcum and ascending colon are affected.

H. G. Rudner (1935) considers that the regions of the intestine are affected in the following order: pelvic colon and rectum, descending colon, cæcum and ascending colon, transverse colon and terminal portion of the small intestine

The *microscopic pathology* naturally varies very much according to the stage to which the morbid changes in the bowel-wall have advanced. The earliest changes appear to be caused by emboli and infarcts in the wall of the colon accompanied by dissolution of the mucosa immediately adjacent, as noted by L. A. Buie and A. A. Humphrey. The earliest microscopic changes recognizable are small

is affected in varying degrees,

The writer has paid speci of *ulcerative colitis*, and has ta the intestinal tract of fatal cases, om various hospitals and institutions. He has also compared the histology with that of a parallel series of proven cases of bacillary dysentery.

most frequently occurs is between the second and third, the next most common, between the third and fourth In children, the prognosis is especially bad, but J A Bargen and J W Kemble hold that below the age of twenty, ulcerative colitis is rare, they had one patient under nine



P H M B

Fig. 76.—Microscopic section of ulcerative colitis, showing destruction of mucosa, with vascular engorgement and cellular reaction in submucosa.

'o the
group
with

As compared with the adult group more children have severe or fulminating symptoms at the onset of the disease.

[illegible] dysentery.

S Lups (1935), and others have called attention to shrinkage and shortening of the large intestine. This occurs particularly in the descending colon, but in a few cases the cæcum and ascending colon are affected.

[illegible]

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In the ulcerated stage, large numbers of diplostreptococci and other micro-organisms are observed in the walls of the colon, and Vimtrup has noted at the edges of the ulcers masses of leucocytes and a zone of fibrinoid necrosis. The muscularis is well preserved, and the serosa is affected in varying degrees, being, as a rule, hyperæmic. (Fig. 76)

The writer has paid special attention to the histopathology of ulcerative colitis, and has taken every opportunity to examine the intestinal tract of fatal cases, as well as specimens obtained from various hospitals and institutions. He has also compared the histology with that of a parallel series of proven cases of bacillary dysentery. As a result of this study he regards the histopathology of ulcerative colitis as distinctive and differing from that of the other disease. The following are the main points :—In ulcerative colitis the onus of the [illegible] Auerbach's plexus are specially attacked.

Biochemical observations —R. Goiffon has studied the biochemical aspect of the disease, but his observations do not go far to clarify the situation He finds that the biochemical picture is dominated by the



1



2



3 *Photos Dr G Mather Cordiner*

1, Radiograph of barium enema in acute ulcerative colitis, showing complete disorganization of mucous membrane. (Death six months from onset) 2, Barium enema of ulcerative colitis showing ulcer niches in rectum and mottling indicating polypoid condition and attempts at repair. 3, Barium enema of ulcerative colitis subsequent to ileostomy, to show stenosis and contracted polypoid colon

ULCERATIVE COLITIS

PLATE XVII

three months. A certain proportion, however, after temporary improvement, drift into the chronic form.

In the *chronic form*, there is persistent diarrhœa which varies little from day to day; there are practically no remissions, or periods during which a solid motion is passed. The fæces are often soft and brown; there are no solid particles, and mucus and blood are present in a varying degree. Gastric symptoms are usually absent—there is no nausea, vomiting, or flatulence, unless they are produced by an unsuitable diet, but hæmatemesis may occur. The tongue is clean, and the appetite remains fair until the terminal stages. On examination, the abdomen is navicular, the colon tender and, on palpation, the sigmoid colon is found to be spastic. Some of the cases progress [illegible]

In those cases in which the disease is progressing, a morbid body-odour may be noted, to which Bargen has drawn attention. This is usually associated with a hopeless and anxious facial expression. Cramps of legs and arms are not uncommon.

[illegible] being entirely unaffected

N. H. Fairley has permitted me to quote the case of a man of thirty-two, who had suffered for six years from mild symptoms with occasional exacerbations. A perfectly normal rectal canal and sigmoid was revealed by sigmoidoscopy, and X rays after a barium enema showed that a condition of pseudo-polyposis was confined solely to the descending colon. It is in cases of this description that partial colectomy has proved successful (Plate XVI.)

[illegible] F. Hurst and F. A. Knott ([illegible]) have described such a case with [illegible]

Nevertheless, however favourably the patient appears to be progressing, there always remains the danger of acute exacerbations which may cause death in two or three months.

A feature of regional ulcerative colitis is that, despite the train of distressing symptoms, the tongue remains clean and the appetite fair. There is usually little abdominal discomfort, apart from continuous diarrhœa, although deep pressure over the course of the large intestine may elicit tender spots, especially in the sigmoid colon, which is usually palpable and spastic.

Complications.—The complications of ulcerative colitis are many and serious. Brust and Bargen call attention to a polypoid condition of the colon which follows ulcerative colitis; in a review of 693 cases, they noted the presence of pseudo-polyposis in 10 per cent, but a further study of the pathological changes in the colons of forty-three patients with chronic ulcerative colitis indicated that the development of true adenomata is frequent. Gallart Mones and Sanjuan have recorded the following complications *diffuse polyposis, stenosis of the rectum and sigmoid, and perforation*. Extracolic complications include arthritis, perirectal abscess, multiple fistulæ, ulceration of the skin, and phlebitis.

Among the 693 cases at the Mayo Clinic, there were sixty-nine with adenomatous polyposis, fifty-nine with strictures, twenty-six with peri-rectal abscess, eighteen with perforation, thirty with arthritis and fifteen with carcinomatosis. Two cases were observed in which carcinomata developed from rectal polypi (Bargen). Independent observers, such as W. I. Wheeler, W. W. Soper, and K. Justi (1921) have noted the same sequence of events. R. J. Jackman, J. A. Bargen and H. F. Helmholz found the incidence of carcinoma of the large intestine was 3.2 per cent for their entire group, but double that for one series of 95 patients in whom colitis began before the sixteenth year.

Bargen has also recorded nephrosis, endocarditis, splenomegaly, ocular disease, hæmorrhage, mesenteric thrombosis, and tetany, multiple complications frequently occurring in the same patient. *This same authority has also noted cutaneous lesions, and Ramel has* recorded a case in which multiple cutaneous ulcers ran a parallel course to a very severe attack of colitis; they were regarded as the outward expression of *severe cytolytic changes in the bowel-wall*. I. R. Jankelson and C. W. McClure (1940) found skin ulceration in seven cases during the height of an exacerbation; all were febrile and toxic. Lowered resistance to infection plays an important part in their ætiology. Local sulphonamide applications resulted in rapid healing. Ulceration of the stomach with gastric hæmorrhage is rare (Heinz).

Carcinoma.—Carcinomatous changes in a colon already the seat of chronic ulcerative colitis are frequent as compared with its occurrence in persons giving no history of any infection. Such microscopic studies as have been made suggest that there is a transition from the adenomatous polypus to carcinoma.

The author has recently had a rapidly fatal case of ulcerative colitis in a man of thirty seven in whom active carcinomatous changes were taking place in the fundi of the glands already partially destroyed by the colitis.

Ocular complications have been noted by B. B. Crohn in the form of conjunctival and corneal inflammation, a condition resembling xerophthalmia.

PSEUDO-POLYPOSIS.—A *polypoid condition is a common sequel of* partial or complete healing in chronic cases, and has been met with frequently since first described by A. F. Hurst. The structure of these



Barium enema of pseudo-polyposis secondary to ulcerative colitis, showing characteristic mottled appearance and sacculation of colon.

ULCERATIVE COLITIS



Photos, Dr G. Mather Cordiner.

Barium enema of chronic tuberculous colitis (T.B. in fæces), showing smooth outline. *Note Stierlin's sign in the cæcum.* Reflex flow from cæcum.

TUBERCULOUS COLITIS

Very offensive liquid fæces are present, intimately mingled with the

examination The presence of pus in the fæces serves to differentiate it from true polyposis

Cytodiagnosis—The microscopic characteristics of the exudate of acute ulcerative colitis cannot always be distinguished with certainty from those of bacillary dysentery. There is a profusion of pus-cells

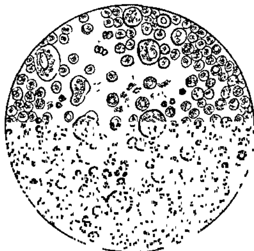


Fig 77—Cellular exudate in acute ulcerative colitis, showing pus and large macrophage cells.

of stiffness In early cases the diffusely granular mucous membrane, and in later cases disseminated mucosal protrusions, can be felt.

Intradermal tests—M. Paulson (1937) has drawn attention to an

pseudo-polyposis may develop in the colon in the absence of any marked symptoms of evident ulcerative colitis.

The author (1938) investigated a case in a young man of twenty years of age who was admitted to hospital in a state of extreme emaciation and anæmia, the cause of which was found by sigmoidoscopy and radioscopic examination to be pronounced pseudo-polyposis. In this instance there was a previous history of abdominal pain of twelve weeks' and of diarrhœa of one week's duration only.

Strictures of the colon are also not uncommon They may develop, without any change in the symptoms, in the course of healing of a chronic case. Sometimes, when a stricture occurs in the rectum—one of the most frequent complications resulting from long-standing involvement (Kiefer)—it may be recognized by sigmoidoscopy; but more usually it is seen by X-rays after a barium enema, when two or more strictures may be revealed. (*See* Table III, p. 18.) Strictures of the ano-rectal region occur in about 9 per cent. of cases (W. D. Smith and R. J. Jackman)

Peri-rectal abscess and fistulæ may develop as the result of infection of the anal crypts, and generally occur during the active stage of the [illegible] W. D. S[illegible] R. J. Jackman

Perforation of an ulcer has been recorded in 8 per cent. of the Mayo Clinic cases, but the Guy's Hospital statistics give a higher percentage.

Multiple *arthritis*, as in bacillary dysentery, is not infrequent. It occurred in 4 per cent. of the Mayo Clinic cases. The author has seen it in three cases, accompanied by fever and affecting numerous joints for periods of two [illegible]

Diagnosis.—[illegible] tion from other [illegible] is not always easy [illegible] tory, must be taken into consideration Pseudo-polyposis has also to be distinguished from polyposis As a rule, the blood-sedimentation rate is high in the former and low in the latter.

The bacteriological investigations of typical stools containing blood and mucus are negative Very often streptococci (*Strept. brevis*) are numerous, and they must be regarded as a concomitant infection; then there is the diplostreptococcus of Bargen, for which special search is necessary (*see* p. 435). The macroscopic characters of the stool vary from day to day and from hour to hour The fæces consist to a great extent of blood and mucus, the former usually predominating

colitis (*see* p 499), or even in malignant stricture. This form is known as regional, segmental, or migratory colitis and is more difficult to recognize than is the usual type It is rare but undoubtedly does occur; its full significance has been emphasized by Bargen and Weber.

The irritability of the affected portion of the bowel, which has been referred to by all writers on this subject, is responsible for "Stierlin's sign"—that is, the shadow of the contrast mass in the normal segments of the bowel is much more intense than in the diseased portion.

In the terminal stages, stenosis of the colon becomes extreme and there is formation of adeno-papillomata (pseudo-polyposis) (Plate XVIII, facing p 443) By the decompression relief, or Fischer's, method, the situation of these granular masses and the occurrence of numerous filling defects can be determined After expulsion of the enema, air is introduced into the bowel and films are then taken These reveal a spotted or marked appearance Sometimes the film gives the impression of a braided band, and the contrast mass attached to the inner half of the bowel may resemble trellis work (Lups). (Plate XVII, 3)

Diagnosis by sigmoidoscopy —Sigmoidoscopy, judiciously performed, affords a valuable means of making diagnosis certain, and is the only method by which the varied changes in the mucosa may be systematically observed

H. F. Bayard (1933), L A. Buie and J A Bargen, and others have drawn attention to the fact that the lesions seen at autopsy do not by [illegible]

infection.

Bayard describes the following characteristics —

1 Glazed granular mucosa which bleeds easily when traumatized.
2 Tubular contraction and thickening of the bowel and rectum (Plate XIX, C)
3 An ironed out, or rounded appearance of the valves of Houston

T. H Morison (1935) distinguishes the following stages .—

1. Diffused hyperæmia (Plate XIX, B.)
2 Œdema throughout the involved area, associated with thickening and friability of the mucous membrane (Plate XIX, D)
3 Formation of miliary abscesses which discharge abundant pus (Lups)
4 The rupture of these abscesses leading to miliary ulcers (Plate XIX, E)

[illegible]

purpuric appearance on the normal pale background.

intradermal test which he believes to be of use in reaching a diagnosis An antigen from the intestinal surface has been prepared which is allied in some way or other to that of venereal lymphogranuloma. Some cases give a positive reaction with the Frei antigen, but this is not to be taken as an indication that ulcerative colitis is of the same nature as lymphogranuloma. The antigen is prepared by making a lysate from *the diseased mucosa with azochloramide in 1 : 10 dilution. Of this,* 0.1 c.c. is injected intradermally.

Radioscopic diagnosis—A study of the essential pathological change which affects all layers of the bowel-wall will lend significance to the radioscopic appearances. In nearly 80 per cent of cases of ulcerative colitis there are lesions of the large intestine extending above the sigmoid flexure, and the radioscopic relief of the damaged mucosa becomes more evident and gross as the inflammatory reaction is more intense.

In preparing the patient for radioscopy, H. M. Weber (1930) has emphasized the necessity for cleansing the bowel of excessive quantities [illegible]

A barium enema should be given, a thin emulsion of barium being used at body temperature As it enters the bowel, attention should be directed to the rectum, for the disease may be confined to this portion only. In early cases no marked radiographic changes may be observed, the only sign may be extreme hyper-irritability, the enema not being retained long enough to permit filling of the colon. The ampulla of the rectum is narrowed and shows a series of coarse and linear striations and, as the disease progresses, the characteristic thickening, contraction, and shortening takes place In advanced cases the colon fills very rapidly and the ileo-cæcal valve is soon reached and sometimes fills The colon itself is narrowed in calibre, and its *length is reduced (H. M. Weber). The course becomes straight, and the* angles at the flexures are converted to right angles. From a soft, pliable, thin-walled tube, it becomes an inflexible, stiff, and straight channel, giving a picture not seen in any other disease of the colon [illegible]

[illegible] are ragged, and when the ulcerations are very deep, many niche-like [illegible]

TABLE XV.—DIFFERENTIATION OF ULCERATIVE COLITIS FROM BACILLARY DYSENTERY

	Chronic Bacillary Dysentery	Idiopathic Ulcerative Colitis
Onset	May be acute at first, often running a relapsing course. Evidence of definite infection	Sudden with sweats. Occurrence sporadic. No evidence of infection
Pyrexia	Irregular pyrexias, but usually apyrexial	Usually intermittent, pyrexia in bouts
Course	Chronic.	May be acute or chronic
Complications	Polyarthritis, parotitis	Polyarthritis, polyposis of colon, stricture, nephrosis, endocarditis, septicæmia, peri-rectal abscess, cutaneous ulcers, splenomegaly
Blood	No anæmia at onset, eventually anæmia. Serum usually agglutinates Shiga or Flexner bacillus	Very severe secondary anæmia from onset. No agglutination
Signs	Usually no tenderness over bowel. Defæcation very painful	Great tenderness. Defæcation usually painless.
Pathology	Serpiginous ulceration of large intestine, localized formation of granulation tissue	Commences in rectum, degree of ulceration varies greatly in different stages of the disease
Microscopic	Chronic diarrhœic stool with undigested particles, occasionally blood and mucus	Red blood cells in clumps. Disintegrating pus cells and intestinal epithelial cells
Sigmoidoscope	Bleeding granulation tissue with rigidity of bowel wall	Granulation, diffuse inflammation of rectal wall, with narrowing of the lumen. Miliary abscesses and ulcers
Sequelæ	Localized stenosis of bowel. *B. coli* complications	Generalized stenosis or bowel perforation, hæmorrhage, endocarditis, and septicæmia.

S Lups has emphasized the large amount of pus which, out of all proportion to their size, may exude from miliary abscesses. It is a fact that the amount of pus which wells forth from the ulcerated surface is often so large that it gives the impression that a large pericolonic abscess is situated in the neighbourhood of the sigmoid and is discharging its contents into the lumen of the bowel.

that dilatation of the rectum becomes painful.

In concluding the section it should be noted that there are some authorities, notably H. L. Tidy, who deprecate the routine use of sigmoidoscopy and radiology
to which they may give rise.
easily made on clinical grour
any other method.

Differential diagnosis —The differential diagnosis has to be made from all other dysenteric diseases in which blood and mucus is abundant in the stools. The difficulty arises chiefly with bacillary dysentery *of the subacute or chronic form. The main points are set* out in Table XV, p. 449.

TREATMENT

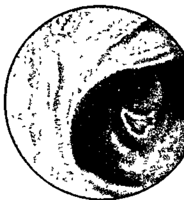
few will disagree

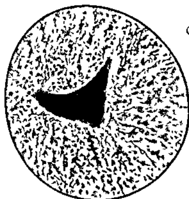
In the main, those who have been especially active in the treatment of chronic ulcerative colitis can be divided into three groups. 1, those who believe that the condition is an infective process and advocate its treatment as a chronic, severe, and debilitating infection; 2, those who believe that it is metabolic in origin and who search for some underlying deficiency, and 3, those who believe "colitis gravis" to be a surgical problem

The old saying that "affections of organs above the diaphragm tend to optimism, and those below to pessimism" was never better exemplified than in ulcerative colitis

Serum and vaccine treatment.—Since 1928 Bargen has been the protagonist of treatment based upon the consideration that ulcerative colitis is an infectious disease of the large intestine, and he has, apparently, had great

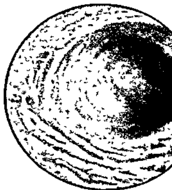












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SIGMOIDOSCOPIC APPEARANCES

PLATE XIX

PLATE XIX

SIGMOIDOSCOPIC APPEARANCES

A. **Acute Ulcerative Colitis.**—Showing plum coloured, easily traumatised mucosa in the second stage.

B. **Tuberculous Ulceration of Rectum.**—Case in which tubercle bacilli were found in material obtained through the sigmoidoscope. The patient was suffering from chronic diarrhœa with blood and mucus in the stools.

C. **Acute Ulcerative Colitis.**—First stage. Usually called hæmorrhagic colitis.

D. **Ulcerative Colitis.**—Superficial ulceration in the third, or ulcerative, stage.

E. **Mucous Colitis,** showing the pale colour of the mucosa and the masses of adherent mucus.

F. **Acute Ulcerative Colitis.**—Early stage, showing granular mucosa, with purulent exudate covering the surface. Note the lack of normal folding of the mucosa.

F. Smek writes that in colitis gravis the beneficial effects of blood-transfusion were first noted by Rachwalsky and H. Strauss, and that this form of therapy has been employed in Austria and Germany by

consequent reaction was most severe.

The writer considers multiple blood-transfusions to be a valuable therapeutic measure. He has had some good examples of its beneficial effects in his practice (summarized on p. 463) H L Tidy, who has adopted a sceptical attitude regarding medicinal measures in this

emulsion of *B coli*) given intravenously A strong systemic reaction is followed by favourable results

but when administered in rectal retention enemata (7–10 gm in 7 oz of water, suspended with mucilage or gum acacia) it has yielded to the

five years duration has now remained free from

recently been favourably reported upon in America, appears to exert some action in controlling hæmorrhage The author has noted improvement recently in advanced cases, but the preparation is not by any means agreeable to take and has a depressing effect In one particularly successful case 2 tablespoonfuls were taken twice daily for 14 days, with the result that the blood and mucus, especially the latter, disappeared and the motions became formed The general condition improved enormously The metallic taste can be [illegible]

Intrarectal medication.—Bismuth subgallate (dermatol), on account of its soothing properties and its hæmostatic action, has been employed by many workers as an insufflation or injection into the bowel. It is first mentioned, in 1909, by Hawkins, who used it in the [illegible]

the diseased mucosa and acts both as a protective and as a soothing agent.

For granular rectitis Lockhart-Mummery has applied nitric acid to [illegible]

[illegible] obtained good results in six cases, with resulting remissions lasting as long as two years The best results were seen in those cases with shortest previous histories This treatment is combined with Iso-gel (Allen & Hanbury) by the mouth Retention enemata are not commenced till the diarrhœa has been checked with opium. D Smith

cit.), but since 1934 has been treating cases of colitis gravis with ascorbic acid,

injections of mercurochrome intravenously are of considerable value in

should, of course, be carefully watched.

Calcium and parathyroid —B Haskell and A Canterow consider that the

[illegible]

In the after treatment reliance should be placed chiefly on kaolin and charcoal, as a method of relieving symptoms

Insufflation of the rectum has been employed, using powders such as the following Dermatol (bismuth subgallate) fifty parts and tannic acid and sodium chloride five parts each, or talcum ten parts with dermatol or xeroform five parts each Bismuth subnitrate and tribasic calcium phosphate, 1–2 drachms, and kaolin, 1 ounce, three times daily, are recommended by Bargen In cases with achlorhydria, diluted hydrochloric acid is used, and when the disease is associated with profound anæmia, iron in large doses, such as ferrum redactum, 3–6 grammes daily (Schotmuller), may be employed For tenesmus, suppositories containing the following ingredients are recommended —

Ext bellad	0 2 grm
Dilaudid	0 003 „
Ol. cacao	2 „
Bals peruv	0 15 „
Ext hamam	0 03 „
Calc chlorid	0 05 „

D C Hare has recorded successful treatment with liver injections combined with massive doses of iron

General summary of effects of medicinal treatment —Amid the welter of therapeutics which have been applied and have already been described, some attempt must be made to lay down certain main lines of treatment In the author's experience, blood-transfusion is of first importance in building up the patient's resistance and in combating both the mechanical loss of blood and the toxæmia. Again and again, it has proved the means of saving the patient's life (*see* p 463) The best results are undoubtedly observed in those cases in which anæmia is a prominent factor

The following are the medicinal measures which have been found useful in practice at the Hospital for Tropical Diseases

To check diarrhœa —Kaolin in some form or other · probably the best form is Kaylene oil, which contains liquid paraffin and kaolin; Kaldrox (one drachm three times a day) is also a good preparation

When *pain* is a prominent feature, opium combined with chalk in the following mixture affords relief —

R Tinct opii	5 min
Ol ricin	3 min
Mist cret ad	½ oz

Half an ounce to be given four hourly

or

amount till the maximum of eight ounces is reached. The injections are given daily. The colon is cleansed with a pint of warm water, and this is followed, after an hour, by a retention enema of three to five ounces of kaolin and aluminium hydroxide in 90–150 c c. of warm distilled water

B. B Crohn and B D Rosenak recommend retention enemata of neutral acriflavine in strength of 1 . 4,000 normal saline as a daily routine, but they add that when it appears to give more irritation than relief it should be discarded Lups has tried enemata of 2-per-cent. boric acid solution, potassium permanganate, ichthyol, bismuth carbonate (½–1 per cent) silver nitrate, protargol, and camomile and tannic acid 1 . 100 In cases of persistent bleeding from the rectum, as in the localized stage of granular rectitis, tannic acid suppositories (three grains acid) have been found, in the author's practice, to be most useful

Vitamin A —Rachet and Busson consider the application of carotene an efficacious treatment It is given in disoxygenated olive oil (Byla), with a few drops of laudanum, in 2–3 c c doses applied direct to the ulcerated surface after a cleansing enema

Antivirus treatment —Antivirus (Besredka) is a filtrate of a medium in which streptococci and staphylococci have been grown for a long time E. J. Oesterlin, A W Johnson, Kinsey, and T Willett have employed the substance as a … enema and then

six normal persons, then transplanted them into broth with glucose, and injected the cultures as an enema twice daily into the bowel of six patients, who were greatly benefited

Additional intrarectal measures —H L Tidy has on several occasions … methods of

a week.

each week on alternate days

In the after-treatment reliance should be placed chiefly on kaolin and charcoal, as a method of relieving symptoms

Insufflation of the rectum has been employed, using powders such as the following. Dermatol (bismuth subgallate) fifty parts and tannic acid and sodium chloride five parts each, or talcum ten parts with dermatol or xeroform five parts each Bismuth subnitrate and tribasic calcium phosphate, 1–2 drachms, and kaolin, 1 ounce, three times daily, are recommended by Bargen In cases with

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six normal persons, then transplanted them into broth with glucose, and injected the cultures as an enema twice daily into the bowel of six patients,

hours, and not more than four a week These enemata should be continued until the number of stools has been reduced to five or six a day.

In the second stage, when the irritation in the colon has been reduced, simple colonic washes consisting of 1,200 c c of normal saline are employed These are run in from a glass funnel not more than one foot above the level of the rectum, and should take at least twenty minutes to administer. The injection of them should never be hurried Three or four of these washes should be given a week.

Sedatives.—

Chloretone, 10 grains

Tinct. opii, 10 minims

Pulv. ipecac co., 10 grains

The application of bismuth subgallate in olive oil, especially in chronic cases, has already been dealt with.

Psycho- and physio-therapy.—The psychological aspects of ulcer-

[illegible]

Dietetic measures.—It has lately come to be realized that starvation diets have no place in the routine treatment of ulcerative colitis. The colon normally functions as a storehouse for substances which are later expelled; the best foods are those which are well absorbed by the small intestine. Some authorities commence treatment of the acute stage by withholding all food for two days. Rankin, Bargen, and Buie consider that, in a diet for chronic ulcerative colitis, the main requirements are that it shall be nourishing and of low residue—furnishing from 2,000 to 3,000 calories—and shall be given in as attractive a manner as possible. Milk, it is generally held, is not well tolerated in the acute stages, but can be added later when absorption is better established.

The *bland diet* consists of: Cereals, two slices of lean bacon, one

[illegible]

seven to twenty medium-sized apples are needed per day. They should be peeled and cored, and then chopped up so small as to go brown. Three to ten ounces of this purée are given at each of four meals in the day for two days, during which time no other food at all is taken, except weak tea if the patient is thirsty.

Gradual transition back to normal diet is effected by the following scheme:

Breakfast.—Tea, or cocoa made with water, rusks, stale bread, small amount of butter.

Midday.—Meat broth free of fat, lean meat or ham, purée of potatoes, bananas, rusks, stale bread, cheese.

Tea.—Tea, rusks, small amount of butter.

Evening.—Same as midday.

℞ Pulv. ipecac. co.	. . . .	10 gr.
Salol.	. . . .	10 gr.
Sod bicarb.	. . . .	20 gr.
Bism. subnitras.	. . . .	25 gr.

In powder form.

To alleviate spasm and tenesmus the following prescriptions have been found useful :—

1. ℞ Tinct. bellad	. . . . . .	6 min.
Sod. brom.	. . . . . .	5 gr.
Elix takadiastase sed.	. . . . .	1 drm
Mist. mag. hydrox	. . . . .	1 drm
Aq. menth. pip. ad.	. . . . .	½ oz

Half an ounce to be given four hourly.

2. ℞ Bism salicyl	. . . . . .	15 gr.
Salol	. . . .	5 gr

In powder form, three times a day.

3 ℞ Pulv. ipecac. co.	. . . .	10 gr.
Salol.	. . . .	10 gr.
Sod. bicarb.	. . . . . .	20 gr.
Bism. subnitras.	. . . .	30 gr

In powder form, three times a day.

4. Starch and opium enema	. . . . .	4 oz

To relieve colicky pains and as an antispasmodic, Rivanol retention enemata, 4 ounces to be retained one to two hours, are useful. Rivanol (2-ethoxy-6 9 diamino-acridine-lactate) is given in a strength of from 1 : 2,000 to 1 : 500 It is credited with a general antiseptic action on pus-producing cocci—strepto- and staphylococci It is incompatible with acids and with normal saline.

To relieve flatulence —

Medicinal charcoal (Bragg).
Charkaolin (Allen & Hanbury)
Pepain, bismuth and charcoal tablets (Boots)

To check intestinal bleeding —

Tannic acid retention enemata (10 ounces, containing 5 per cent tannic acid).
Tannic acid suppositories (tannic acid, 3 grains)

For anæmia —

Blood transfusion.
Large doses of iron ferri et ammon cit, 30 grains three times daily
Eatan (a muscle and beef extract made by Fassett and Johnson), one teaspoonful in half a tumberful of water four times daily.

General stimulant.—

Intravenous injections of glucose, 5 per cent, in normal saline 10 ounces.
Intravenous injections of calcium gluconate (Sandoz) 8 ounces.

means of continuous drainage

rectum

The operation is performed as follows —

lar mesentery

5 None of the appendix is removed, but a rubber appendicostomy catheter is inserted into its lumen, passed into the cæcum, and held in position with a catgut suture

6 After seven days the unwanted portion of the appendix is excised An appendicostomy must not be performed if the appendix is fibrosed or *very short*

Irrigation should be performed twice daily, the best solution for this purpose being normal saline, under about 1½ foot of pressure

in which all other remedial measures have failed to afford relief The results are often brilliant, and it is unreasonable to assume that it is not justifiable in any circumstances

M Donati considers that ileostomy, cæcostomy, and colostomy of

One of these meals is substituted each day for one of the apple meals until the patient is no longer having any apples, and then a slow return to normal diet is made.

A preserved apple powder is sold under the name of *Aplona*.* This contains an astringent principle and is always ready for use. It is said to exert a specific action on the mucous membrane

Salt deficiency in ulcerative colitis.—Salt deficiency is common in ulcerative colitis, as it is in Addison's disease, pyloric stenosis, excessive sweating, diarrhœa, and vomiting C. S Welch, M Adams, and E C. Wakefield of the Mayo Clinic have shown that in ulcerative colitis the deficiency is due to the response of the body to a forced and continuous loss of protein material. In this condition the blood-urea tends to be low, pointing to a small katabolism of amino-acids, and indicating that all the available amino-acids are being utilized for the synthesis of the protein which is being lost. The urea-nitrogen consequently forms much less than the normal 70–80 per cent. of the total nitrogen leaving the body.

Hence, it is well to point out, a diet liberal in proteins is necessary in ulcerative colitis.

The following is a specimen of *high-protein diet* for ulcerative colitis:

First Stage.

Breakfast—4 oz. fish, 1 egg and 1 egg-white, 3 oz. skimmed milk, bread, butter, tea, sugar.
11 *a m*—5 oz. skimmed milk, 1 egg
Midday—5 oz lean meat, 6 oz skimmed milk, 1 egg-white, potatoes,

pudding.

Second Stage

Breakfast—5 oz. fish, 1 egg and 2 egg-whites, 3 oz. milk, bread, butter, sugar, marmalade, orange.
Midday—4 oz lean meat, 5 oz milk, 2 egg-whites, potatoes, orange.
jam, sugar
te, potatoes, bread, butter, fruit, 1 egg.

Surgical measures—When medical measures have failed—and this occurs, it must be confessed, in a fair proportion of cases—or when complications ensue, as they so commonly do, then **surgical drainage** must be employed. The nature of this drainage varies

ough
much
many
and

* Coates & Cooper, 94 Clerkenwell Road, E C 1.

cases of this severity the greater portion of the large intestine is involved, so that eventually ileostomy becomes necessary

Prognosis.—It is difficult to predict, with any degree of accuracy,

Mortality rate—In a discussion held at the Royal Society of Medicine in 1909, it was recorded that, out of 288 cases collected from the records of seven London Hospitals, 50 per cent had died In 1928, Bellingham Smith reported that twenty-four out of his forty-six hospital cases had died (52 per cent) Recent statistics are rather better According to L S Kilbrick and R H Miller, who record a series of 149 cases, the mortality rate is 18 per cent In twenty (74 per cent) deaths followed some operative procedure, deaths also occurred from peritonitis, widespread sepsis, and local disease, such as pneumonia T L Hardy and E Bulmer record thirty-one deaths in a series of 104 cases, seventeen in male and fourteen in female patients, and they

anuria, one Perforation of the colon constituted one of the commonest forms of death; in two cases more than one perforation was present Perforation of the ulcer may actually occur without causing general peritonitis

The expectation of life appears to be fairly good in private institutions, as E I Spriggs's (1931) statistics at Ruthin Castle show a mortality rate of only about 12 per cent

A F Hurst, at New Lodge Clinic, 1921–34, has treated some forty patients with very favourable results, the mortality rate in this series

a life of normal activity There is always a very great tendency to recurrence Relapses are apt to be brought on by superimposed infections, especially tonsillitis, and by fatigue or mental strain Hurst has pointed out that in younger patients the colon, when examined after giving an opaque enema, may show an abnormal appearance, and yet the patient may not have suffered from diarrhœa for years

the ascending colon may any of them be indicated, according to the nature of the case. Partial colectomy can be performed; but total colectomy is absolutely contra-indicated.

Ileostomy—L S Kilbrick and R. H. Miller, in recording twenty-nine recent cases, covering a period of ten years, in which ileostomy had been performed, recommend this as the only operative measure which should be seriously considered Of these twenty-nine cases, ten have required a further operation of total or subtotal colectomy. The indications for colectomy are said to be polyposis, recurrent attacks of fever, malaise, and continued anæmia Both operations—ileostomy and colectomy—should be preceded and followed by blood transfusions

Bargen, Brown, and Rankin have reported eighty-two cases, ranging in age from seven to sixty-one years, in which ileostomy has been performed The most beneficial type is the one-barrel ileostomy They consider the results of this operation to be satisfactory, especially when performed to relieve the chronic complications of the disease, but they recommend that it should *not* be performed in uncomplicated cases, unless other forms of treatment have been thoroughly tried From their extensive experience, they do not consider that any [illegible]

cases of colectomy for diffuse pseudo-polyposis and other complications of chronic ulcerative colitis. In four, the colon was removed down to the recto-sigmoidal junction, and in the other, total colectomy was performed. Rectal polypi were treated by vigorous fulguration

H. W Cave and W. F Nickel (1940) have reported upon 80 ileostomies with 7 deaths (mortality rate 23 per cent) This rate is as high as 45 per cent. in emergency ileostomy. This operation should not in itself be regarded as a curative process, they hold, but as the first step in the complete removal of colon and rectum

[illegible]

permanent He considers that aseptic technique is extremely important, as in long-standing cases of ulcerative colitis there is a great influx of pathogenic bacteria into the colon and terminal ileum.

R B. Cattell considers that transverse ileostomy is the operation of choice and is of great value in chronic cases. W. Weissenborn (1939) has reported the successful removal of the colon from cæcum to anus The patient, a man of 18, recovered with a permanent ileostomy opening

In cases of extensive peri-rectal abscesses or rectal strictures, colostomy may be required for temporary drainage, but usually in

to have only three-fifths as many relapses as the patient of under twenty

Once the disease has made its appearance, the mucous membrane and indeed all the layers of the bowel-wall are permanently altered, and in the healing process swellings, polypi, and strictures may form Even when such strictures interfere with the passage of the normal fæcal contents, no special tendency to relapse appears to be induced

may only result in bringing about a severe relapse

According to the studies made by E D Murray, psychological and hysterical stresses appear also to be predisposing factors during the third and fourth decades of life.

Summary of the author's series of forty cases of ulcerative colitis (1920–37)

This resumé gives, in succinct form, some of the facts to which reference has been made in the text

Sex males, ten, females, thirty Average age twenty to thirty eight, eldest fifty Deaths in hospital two (5 per cent) Residence abroad nine only, in India, Ceylon, Australia, and South Africa All clinical degrees of severity were noted

P

but it appeared to be entirely beneficial, as the disease, which had lasted for four years, ceased, and she returned to Burma in good health (Chart 14)

X rays after barium enema, fistula opened into the vagina, but healed without surgical interference She recovered on each occasion after repeated blood transfusions, and is now (1937) well, with no anæmia, or any external symptoms

patient

Appendicectomy, one case, in which pathological appendix was demostrated and removed with considerable benefit to the patient.

Valvular cæcostomy, one critical case, in a woman of thirty-four, who

Hurst has given the following table from his own statistics as well as those of E. Spriggs.

Well or carrying on . .	66	(77.6 per cent)
Not well . . .	9	(10 6 „)
Ill . . .	2	(2.4 „)
Dead . . .	8	(9.4 „)

Of the 66 recoveries, 38 had no relapses, and 28 had relapses from which they recovered

Duration of the disease.—T. L Hardy and E. Bulmer, in their series of cases from the General Hospital, Birmingham, found that the case of shortest duration—a fatal case—lasted six weeks, and, at the other extreme, there was a patient suffering from the intermittent type of the disease who succumbed eventually after thirty-six years

According to these authors, the most unfavourable type of case is the one showing an acute onset, and the most favourable the one characterized by intermittent attacks with complete freedom in the intervals

Relapses—Banks and Bargen (1934) discourage an unduly optimistic state of mind when the treatment appears to have been successful at the termination of the attack The joy of the patient will not be shared by the wise physician, who, basing his knowledge upon the fundamental pathological changes in this disease, will realize that the condition may recur

The histories of 232 consecutive cases of chronic ulcerative colitis in the Mayo Clinic have been analysed; 209 patients had received *medicinal treatment and twenty-three had been previously subjected* to some form of short-circuiting operation In 140 patients no less than 276 recurrences of colitis were noted Infections of the upper part of the respiratory tract were held directly responsible for the great majority, but an appreciable number (12 per cent) were associated with conditions which traumatized or increased the irritability of the gastro-intestinal tract

Immunization against diplostreptococci was carried out as a routine in the treatment, and this appeared to be an infrequent cause of the reactivation of a quiescent colitis In 3 3 per cent of patients this occurred before the fourth injection of vaccine, usually it followed the first

Recurrences after abdominal operations were rare, but four were secondary

The seasonal incidence of relapses has also been noted; there is a definite tendency for the relapse rate to be lowest in the summer months The tendency to relapse was found to decrease with age, so that in the same period of time the patient over forty may be expected

descending colons had taken place, the general condition of the patient once more improved, and blood regeneration quickly took place In October, 1935, he weighed 12 st 4 lb, and was comfortably fitted with a colotomy belt No excoriation of the skin was noted In



Fig 78 – Very acute case of ulcerative colitis Appearance of patient three months after ileostomy



Fig. 79.—Appearance of the same patient before operative treatment.

February, 1936, he was re admitted with intestinal hæmorrhage, proceeding from pseudo polypi which had formed in the sigmoid colon,

had suffered for seven years, she was 3½ months in hospital, and was lavaged daily with six pints of saline through cæcostomy opening Great clinical improvement, discharged with colotomy belt

79
dy

April, 1935

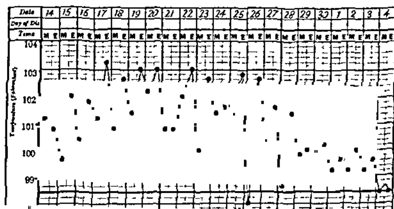


Chart 14.—Pyrexial bout during convalescence from ulcerative colitis. The patient remained subsequently free from symptoms for three years. (See text.)

Valvular

the patient became critical

It had not been realized at this time how rapidly stenosis of the

was found that an advanced degree of stenosis of the transverse and

Stomatitis is the earliest symptom of excessive therapeutic use or of chronic poisoning It occurs as readily when mercury is used by inunction or injection as when it is taken by the mouth Fetor, a metallic taste, soreness of the gums, and salivation (ptyalism), are its accompaniments If the mercuric dosage is pushed further, the gums blacken and, later again, the tongue swells and ulcerates In a chronic case of severe poisoning all the teeth may be lost and necrosis of the jaw may ensue

The mechanism of stomatitis and colitis is thought to be connected with the precipitation of mercuric sulphide which takes place in the capillary endothelium in the mouth and colon, the sulphide being formed by the interaction of putrefying material with the circulating ionized mercury It is toxic to the cells with which it is in contact, and the injured necrotic tissue furnishes a starting-point for ulcerative micro-organisms, especially *B fusiformis* and *Spirochœta dentium* and, in the large intestine, *Bacillus coli*

The symptoms of mercurial colitis may greatly resemble those of ulcerative colitis , there is the same passage of blood-stained muco-pus, together with pain and tenesmus At other times the symptoms are those of a chronic and uncontrollable diarrhœa *

In urological literature specific instances are to be found in which symptoms of acute ulcerative colitis have supervened upon some simple urological operation such as cystoscopy A series of such cases have been reported in recent years A L d'Abreu and A C Lysaght (1936) recorded three The onset was as sudden as it was unexpected, for the subjects were healthy men without any suspicion of renal inflammation Two were fatal and the colon showed an extraordinary degree of recent hypertrophic ulcerative colitis, the mucous membrane smelling strongly of ammonia In a second paper in 1936 these same authors put forward the idea that undue susceptibility to mercury might possibly be the determining cause, as the instruments used at cystoscopy had been [illegible]

[illegible] agent In two, diagnosis of mercurial poisoning was arrived at during life and proof was obtained of the presence of this metal in the organs post mortem

Acute mercury poisoning after cystoscopy might possibly be due to mistaken use of a too-concentrated solution, abnormal circumstances leading to excessive absorption, or idiosyncrasy When the morbid changes in the bladder are unusually severe this may aid absorption There is now no doubt that oxycyanide of mercury in examinations of the urinary tract is highly dangerous

* In lead poisoning the most prominent symptoms are "lead colic," a paroxysmal pain eased by pressure, together with oliguria and obstinate constipation In arsenical poisoning there is vomiting first and then acute diarrhœa resembling cholera

CHAPTER XXV

MERCURIAL COLITIS, URÆMIC COLITIS AND OTHER FORMS OF TOXIC COLITIS, INCLUDING THYROTOXICOSIS

MERCURIAL COLITIS

MERCURIAL poisoning in its clinical manifestations may be divided into three stages: (*a*) the *acute*, which generally takes place in suicidal cases from an overdose of mercuric chloride; (*b*) the *subacute*, usually occurring from therapeutic overdosage, for example, during

mercury vapour makes efficient protection difficult.

The immediate effects of mercurial poisoning are due to coagulation, irritation and superficial corrosion to which the mucous membranes are susceptible

tion, burning

mouth and ph

involved, and within three days the urine becomes scanty, with albumin and casts. Anuria becomes established and death may ensue within one week.

Pathology.—The macroscopic and microscopic appearances of the mucous membrane of the large intestine resemble those of severe ulcerative colitis. There is hæmorrhagic congestion, and coagulation necrosis leading to ulceration. The kidneys exhibit the appearance of acute nephritis, often with calcification of the epithelium of the convoluted tubules.

This pathology is interesting in so far as it has a bearing on the

working on
by the colon,
of mercury
excretion of

within three minutes, but should this be delayed for
toxic phenomena set in. Other soluble mercuric salts, the chloride, iodide, and cyanide, have approximately the same toxicity, though the toxicity of organic compounds with firmly bound mercury is relatively low.

Ether [illegible] dissolved in saline in the form of a rectal [illegible]

in the intestines, urgent tenesmus, diarrhœa, sometimes dysenteric in character "

Used as a 5 per cent solution in warm normal saline, apart from technical difficulties, more success has been obtained but Arnd describes diarrhœa in his cases

Ether in oil (olive or carron) seems, however, to be free from the objection of causing irritation of the bowel and Gwathmey, using a 75 per cent solution, claims to have had no trouble Hatcher advocates a 50 per cent solution as the maximum strength on account of the fear of colitis but, from experience of some hundreds of cases, Mennell reports that no trouble need be anticipated in the rectum from the use of a 60 per cent solution of ether in olive oil The ensuing anæsthesia has, however, to be supplemented

Paraldehyde given per rectum is extensively used as a preliminary narcotic for children, but it is used only in such a way as to induce sleep, anæsthesia then being procured by other means A 5 and 10 per cent solution in saline is frequently given in doses gauged by body weight Any proctitis following such doses is negligible, though slight tenesmus has been said to occur

Avertin is nowadays used most extensively and is given by the rectum in a 2½ per cent solution in doses calculated by body weight (0 1 gramme per kilo) It is tribromethyl alcohol and is unstable in solution, readily decomposing into toxic bromine compounds which are very irritating to the intestine It must be freshly prepared for every patient and dissolved in distilled water at 113° F (45° C), and the solution must be tested with Congo Red before use Cooling allows crystals of avertin to be precipitated and warming leads to its decomposition

If due care is taken in the preparation of the solution, irritation of the rectum very rarely occurs and is then only transitory In a series of 5,000 cases published by L B Mueller, there were only two cases of rectal trouble One was a minor incident, but the second was more serious, necrosis of the intestinal mucous membrane being found

DISEASES OF THE THYROID

Thyrotoxicosis —Among the many clinical manifestations of thyrotoxicosis, chronic diarrhœa is a feature, it may indeed consti-

diarrhœa, which often coincides with exacerbations of nervous mani-

Treatment.—The first essential, when mercury has recently been *taken by the mouth, is to* produce emesis. Milk and calcium sulphide by the mouth should subsequently be given in large quantities, also enemata containing 10 per cent. sodium thiosulphate. A popular antidote is three raw eggs and a quart of milk followed by gastric
ctive; sodium
ogen peroxide,

URÆMIC COLITIS

In the uræmic state, whether produced by the intrinsic condition of the kidneys or the accompaniment of some other disease, gastro-intestinal symptoms are extremely common. Diarrhœa is associated with

statement made in most textbooks of general medicine. Little or no original investigation into this infrequent complication appears to have been undertaken

There is considerable evidence that violent inflammatory disturbances of the alimentary tract do accompany both acute and chronic urinary disturbances. The lesions of the mucous membrane appear to be caused by the excretion of urea through the intestines *In their* pathology and general appearance they resemble ulcerative colitis. (Plate XV, 1, facing p 484.)

COLITIS FOLLOWING RECTAL MAGNESIUM SULPHATE

In the pre-operative treatment of many forms of cerebral disease with high cerebro-spinal fluid pressure, for example, in brain abscess, a 25 to 50 per cent. solution of magnesium sulphate is often given per rectum four to six hourly for one or two days, with the object of reducing pressure temporarily so that an operation can safely be performed A certain percentage of such patients develop definite
In such

ETHER AND AVERTIN COLITIS

anæsthesia
duce proctitis
erved in their

Affections Resembling Dysentery

festations. It may, however, occur independently In the most severe type, rapid exhaustion follows upon the passage of numerous diarrhœic stools, as in cholera; and dehydration is soon set up. When in doubt regarding the true nature of troublesome vomiting, iodine should be given intravenously, as it is usually followed by amelioration of symptoms

It cannot be said that there is anything characteristic about the diarrhœa of thyrotoxicosis. The fæces are usually liquid, pale, and off
of
ma
the mucosa.

A man of forty-eight, who for many years had

pressure of 80 There was also a faint fine tremor of hands and tongue. The stools were diarrhœic and pale On sigmoidoscopy, no lesion of the mucous membrane could be observed

Treatment with small doses of tincture of iodine was instituted, with immediate improvement The diarrhœa ceased, the stools became normal, and the patient put on weight at the rate of 3 lb. per week

Hypothyroidism.—It is not generally realized that hypothyroidism, or myxœdema, may produce the dysenteric syndrome, but one interesting example of this has been encountered

In 1924, the wife of an English officer in India was examined. She was

abortions in three years

It was very clear after a brief examination that she was in a state of hypothyroidism, complaining of chronic aching pain in head and right arm, while her knees were so weak that they often gave way on descending stairs She was also subject to recurring chilblains Her face was puffy, hair brittle, lips were slightly cyanosed, and nails fragile, and longitudinally ridged. Speech was staccato

The blood and mucus in the fæces were probably derived from stercoral ulceration of the sigmoid and rectum, due to the chronic constipation Extensive necrotic ulceration was revealed by sigmoidoscopy

Improvement on full doses of thyroid extract, 3 to 5 grains daily, was remarkable. All signs of myxœdema eventually disappeared, including constipation, and a month later a second sigmoidoscopy showed that the stercoral ulcers had completely disappeared

filter. When injected into a rabbit, they produce posterior paralysis and rapid death. Sheep are extremely susceptible to inoculation, but are immune to the toxin when given it by the mouth

Pathology.—In the victims of mushroom poisoning subpericardial and subpleural hæmorrhages are seen and all the internal organs are congested. Intense fatty degeneration of the liver, resembling that due to phosphorus-poisoning, has been observed, and parenchymatous degenerative changes are found in the tubular epithelium of the kidneys Severe and widespread damage is seen in the central nervous system, and the brain is, as a rule, congested and œdematous. It is

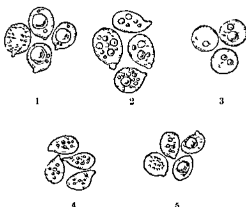


Fig 81 —Spores of poisonous fungi as they may appear in the fæces
1 *Amanita phalloides* 8-9 × 7-8μ, 2, *A verna* 10-11 × 7-9μ, 3, *A virosa*, 8 × 10μ, 4, *A ovoidea*, 10-15 × 5-8μ 5 *A muscaria*, 9-11 × 8-9μ. (*After Dufarric de la Rivière*)

Symptoms.—A number of clinical varieties of mushroom poisoning are recognized :—

Mycetismus gastro-intestinalis —In this type of poisoning violent nausea and vomiting with diarrhœa are the only symptoms Recovery is usually rapid

Mycetismus choleriformis —In this type, violent abdominal pains are followed by nausea and vomiting and usually by profuse diarrhœa Nearly always severe hepatitis with jaundice is also present and toxic nephritis and anuria frequently occur Poisoning of this type is caused by many varieties of Amanita, but especially by *A phalloides*

Mycetismus nervosus —Severe gastro-intestinal symptoms predominate at the onset and are soon accompanied by profuse salivation, perspiration, and lachrymation Mental confusion and delirium occur, usually in fatal cases The fungi which produce this combination of symptoms are those

Mushroom poisoning is due to the ingestion of poisonous fungi of the genus *Amanita* which in some degree resemble the common edible mushroom. Three particularly poisonous species are recognized :—

are colourless (Fig. 80)

Amanita verna (Friès, 1871) Quelet, 1872 The Spring Amanita —This is apparently an early variant of the former species

Amanita virosa (Friès, 1836) Quèlet, 1872 —This is a distinct species with a conical crown which is viscous in wet weather, but satin-like in dry It grows in moist woods The margin of the crown is non-striated, but is lobulated and slightly indented The stem is white, cylindrical, and provided with an

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birch or coniferous woods, and is common from July to December It is very poisonous, but less so than *A. phalloides* An extract of the dried cap was used as a stimulant by many Siberian tribes and its sale was made a penal offence The spores are white, ovoid and spherical, and 9-11 by 8-9 μ in diameter.

About nine other species of *Amanita* are known, but none are so poisonous as these four.

Letellier has devised the following tests for edible and non-edible species —

The edible species give no precipitate in solution with dilute ammonia and with double iodide of mercury and potassium, whereas the inedible fungi *A. phalloides*, *A verna* and *A. virosa* give a violet colour-reaction with sulphuric acid, *A muscaria* gives a light brown colour, *A. pantherina* gives a brown colour-reaction, *A citrina* brownish green, *A. vaginata* pale brown, and *A rubescens* faint purple There are no colour-reactions with *A. junquillea* and *A spissa*

The toxins of these fungi have been extensively studied A viscous substance *viscosine*, or mucilage of the toadstool, is found principally in the epidermis of the crown The species *A muscaria* contains a complex ammonia-derivative, *muscarine*, the action of which closely resembles that of pilocarpine, and a substance termed pilz-atropin, which stimulates the autonomic nervous system and produces an increased secretion from the various glands. *A. phalloides* contains the

limbs in a symmetrical manner. This tendency to bleed is not confined to the skin, but may be intramuscular, periosteal, or intravisceral [illegible]

[illegible]

with intestinal lesions may closely simulate intussusception, and may themselves be complicated by that condition or by peritoneal effusions. The differential diagnosis from the various forms of dysentery is not always an easy matter, as the case here cited indicates

[illegible]

his school

[illegible]

commenced with an arthritis of the left knee later, diarrhœa with blood and [illegible]

containing muscarine, that is *A. muscaria*, and some species belonging to the genera *Clitocybes* and *Inocybes*

Mycetismus sanguinareus—In this type of poisoning gastro-intestinal symptoms occur at the onset; later there is rapid hæmolysis causing anæmia, *jaundice, and hæmoglobinuria* The mortality is low.

Mycetismus cerebralis.—In this form transient excitement with hallucinations and dilatation of the pupils is present. Collapse may occur. Recovery usually takes place

hours or even more; abdominal pains are severe, nausea and vomiting extreme, and diarrhœa is also present.

effect it is important to administer blood or saline intravenously.

Diuretics in the form of potassium citrate should be administered freely, in order to eliminate as much toxin as possible. An antiserum to amanita-toxin and amanita-hæmolysin has been produced, but the results of its administration are inconclusive.

A practical suggestion for treatment has recently been made by Mutch, who advises the administration of medicinal kaolin by the mouth, since the adsorption potency of kaolin for muscarine has been found to be at least 8 8 mg. per gramme. Large doses of colloidal kaolin are indicated.

HENOCH'S AND OTHER FORMS OF PURPURA

Henoch's purpura, also known as anaphylactoid purpura and toxic purpura, probably belongs to the same group as non-thrombocytopenic purpura, the so-called purpura simplex, and peliosis rheumatica (Schoenlein's disease), all of which appear to be manifestations of the same pathological state The term Henoch's purpura is usually restricted to those cases accompanied by urticaria, œdema, swollen

they result from an abnormal permeability of the capillary vessels
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Other Causes of Diarrhœa and Dysenteriform Symptoms

CHAPTER XXVII

CARCINOMA OF THE COLON AND RECTUM, POLYPOSIS, POLYPUS

CARCINOMA OF THE COLON

[illegible]

year Its origin is obscure, but it may arise in benign adenomata,

[illegible]

1, soft medullary adenocarcinoma, 2, scirrhotic carcinoma, or fibro-carcinoma, and 3, mucoid adenocarcinoma.

It has been remarked that the carcinomata of the right half of the colon are large ulcerating growths, and those of the left annular, hard and constricting It is noteworthy also that medullary growths in the right side do not usually produce obstruction, because of the

[illegible]

palpable tumours

Local metastases usually occur in the lymph glands in any part of

inations, and it may, therefore, be said that, as far as this disease is concerned, the radiologist is more important than the pathologist

the colon than is a barium meal

The importance of digital examination cannot be over-estimated, and sigmoidoscopy offers an invaluable method of recognizing growths

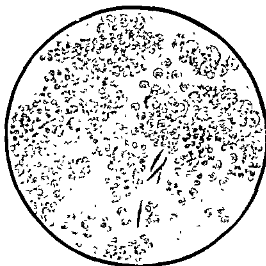


Fig 82.—Appearance of cellular exudate and Charcot-Leyden crystals from a case of carcinoma of the rectum

within the range of that instrument Diagnosis may be aided by microscopic examination of the fæces and a critical observation of the cellular exudate In the author's experience, shed epithelial cells are frequent, while pus cells are comparatively scarce, Charcot-Leyden crystals are commonly encountered, and blood-cells tend to conglomerate in clumps (Fig 82) On the other hand, the cell picture in the stool may not be in any way characteristic

The chief difficulty in diagnosis is that carcinoma is so closely simulated by other tumours of the colon, notably the hyperplastic form of amœbiasis, hyperplastic tuberculosis (p. 502), diverticulitis, segmental ulcerative colitis, polyposis, syphilis, actinomycosis, and retrocæcal appendical abscess Occasionally, also, carcinoma of the

the large intestine, and it is rare to find metastases in the liver without implication of the lymphatic chain in the first instance. It is well known that metastases occur more frequently from carcinoma of the rectum than from any other segment of the bowel.

Symptoms.—The symptomatology is so variable that it is difficult to describe it succinctly. Usually the onset of symptoms is insidious, though rarely it may take place with alarming rapidity. As a rule, there is diarrhœa with the passage of mucus and later of blood; there may be irregularity of the bowel movements, diarrhœa alternating with constipation. It is probably true that any profound change in the intestinal habits of an elderly person demands further investigation, chronic diarrhœa being more suggestive than chronic constipation

Gastric symptoms commonly associated with colonic growths are chronic furred tongue, loss of appetite, and dyspepsia. Borborygmi and visible peristalsis are considered to be early symptoms, but the latter can be recognized only in lean subjects. Pain is often an early symptom, but may be slight and unobtrusive; not unusually it is referred to the epigastrium. Tenesmus is probably present only when the growth is in the lower sigmoid or rectum, and as a rule the lower the growth, the more severe is the straining at stool.

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properly prepared with this object in view.

The duration of symptoms of carcinoma from all parts of the colon is estimated at from fifteen months to two years.

When carcinoma occurs in the right half of the colon it tends to produce a mild dyspepsia resembling chronic appendicitis or cholecystitis, with anæmia and progressive emaciation A mass may then be accidently discovered in the right iliac fossa

of this

viscus.

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ar

There is a tendency to perforation, and local abscess formation is common

Diagnosis.—*The diagnosis of carcinoma of the bowel is by no means easy.* It hinges largely upon differential considerations, and ... usually arrived at by a process of exclusion

are referable to the metastases Loss of weight is usually quite untrustworthy in the earlier stages

It has been generally remarked that growths in the rectal ampulla produce symptoms only when they have attained very considerable size, this is probably due to the space in which they can expand When, however, such a growth ulcerates, the fæces become mingled with

to these structures

teristic that it is hardly likely to be mistaken for anything else The sigmoidoscopic appearances have to be distinguished from polyposis, amœbic dysentery, ulcerative colitis, tubercular disease, and many of the other pathological states described in this book, but there

scopic picture produced by amœbiasis is so characteristic as not to admit of any reasonable element of doubt

Biopsy methods should, of course, always be used whenever possible, portions of the growth being removed for microscopic section One

obviously suffering from amœbic dysentery when at the same time a carcinomatous ulcer was present in the rectum A large indurated rectal ulcer due to amœbic ulceration is also met with occasionally

assumption that, because these crystals are present, the case is necessarily one of amœbiasis An instance of such a mistaken diagnosis may be mentioned .—

stomach and retroperitoneal growths, such as hypernephroma or lipoma, must be considered.

CARCINOMA OF THE RECTUM

Carcinoma occurs much more frequently in the rectum than in any other part of the intestinal tract with the exception of the stomach It occurs much more often in men than in women, and most patients are between forty and seventy years of age, although young persons may also be affected The duration of symptoms is usually shorter than in carcinoma of the colon, and averages less than one year The

Ætiology.—In this situation also it is difficult to surmise the staring point of carcinoma, except to state that it is apt to arise in a polyp Constipation does not appear to be a predisposing factor.

Pathology.—Carcinomata of the rectum develop from the glands of *Lieberkuhn*, and are usually adenocarcinomata. *Those originating* in the anal canal are true squamous-celled growths Adenocarcinomata of the rectum tend to undergo mucoid or colloid degeneration Metastases from rectal neoplasms occur, especially in the liver, generally in proportion to the degree of malignancy

Symptoms.—Rarely do the symptoms such a growth may evoke

of defæcation, or may be intermingled with the fæces as in amœbic dysentery; these are the cases which it is sometimes so difficult to differentiate from other dysenteric diseases. As a general rule, carcinoma of the rectum is not associated with such profound anæmia as is carcinoma of the colon Usually the development of such a growth in the rectum or pelvic colon is associated with some change in the intestinal habits of the patient, or some signs of irritability. Increase of meteorism is one danger signal; sudden attacks of constipation alternating with diarrhœa constitute another. Sometimes the stools are ribboned and otherwise deformed, but this only occurs when a very

usually
and has
ation is

absent. Pains in the sacrum and shooting pains in the hips and thighs

are referable to the metastases Loss of weight is usually quite untrustworthy in the earlier stages

It has been generally remarked that growths in the rectal ampulla produce symptoms only when they have attained very considerable size, this is probably due to the space in which they can expand When, however, such a growth ulcerates, the fæces become mingled with necrotic shreds, pus, mucus, and blood, giving out an offensive odour, considered to be characteristic of carcinoma When the growth has touched laterally adjacent organs, such as the urinary bladder, uterus, or sacrum, these become involved and symptoms are produced referable to these structures

Diagnosis.—The diagnosis of rectal carcinoma is often established by digital examination, but many of the lesions are situated beyond the reach of the index finger, some can be reached better by bimanual examination Usually the only satisfactory measure is the use of either proctoscope or sigmoidoscope The appearance of a carcinomatous growth in the rectum—the typical cauliflower-growth—is so characteristic that it is hardly likely to be mistaken for anything else The sigmoidoscopic appearances have to be distinguished from polyposis, amœbic dysentery, ulcerative colitis, tubercular disease, and many of the other pathological states described in this book, but there appears to be no reason why a mistake in diagnosis should arise, if the various methods described in Chapter I are followed and microscopic examinations of the exudate are undertaken Certainly the sigmoidoscopic picture produced by amœbiasis is so characteristic as not to

in the fæces, because this does not preclude the co-existence of carcinoma The author encountered two cases in which the patient was obviously suffering from amœbic dysentery when at the same time a carcinomatous ulcer was present in the rectum A large indurated rectal ulcer due to amœbic ulceration is also met with occasionally,

[illegible]

[illegible] one of amœbiasis An instance of such a mistaken diagnosis may be mentioned —

A naval officer, 46 years old, stationed in Malta, had been treated for two and a half years for chronic amœbiasis, solely on account of the presence of Charcot-Leyden crystals in the fæces, together with blood and mucus. A digital examination of the rectum revealed a large, fungating, malignant growth, necessitating an abdomino perineal operation (Fig 83.)

Radioscopic methods are of little avail in diagnosis unless the filling of the rectal ampulla is actually visualized on the screen. Obviously



Fig. 83.—Carcinoma of rectum, showing lymphatic spread.
(Preparation by Dr Cuthbert Dukes)

there is no necessity for this method to be employed when the growths themselves can actually be seen

POLYPOSIS INTESTINI

... the colon.
... natosis of the large intestine.
Th... , preferred by Rankin, Bargen, and Buie in their textbook, as indicating more satisfactorily an adeno-
... l from the polypoid forma-
... tuberculosis, bilharziasis,

chronic bacillary dysentery, and often with chronic ulcerative colitis Pierre Augier (1932), who has given the most complete account of the condition, considers that it is identical with colitis polyposa (Virchow, 1860), polyadenoma tractus intestinalis (Skilasowski, 1881), polyposis intestinalis adenomatosa (Hauser, 1895), and polyposis intestini (Ziegler, 1903).

Another important monograph on this disease is by H Tønnesen of Copenhagen (1931) who, in a review of forty cases culled from the whole of Denmark, has shown that polyposis intestini is of the same nature as the similar polypi found occasionally in the stomach

These multiple adenomata are really true neoplasms of congenital origin, are usually familial (as Cuthbert Dukes has so ably shown), and are known to undergo malignant changes in 40 to 50 per cent. of cases

Ætiology —Polyposis is a disease of youth or early middle age Doering recounts the following age incidence in forty cases .—

1–10	years,	2	cases
10–20	,,	10	,,
20–30	,,	10	,,
30–40	,,	13	,,
40–50	,,	2	,,
50–60	,,	2	,,
60–70	,,	1	case

Schöttler's review of ninety eight cases gives much the same proportions

[illegible] developed from [illegible] as gradually de- [illegible] se from certain [illegible] connexion with other epithelial cells [illegible]

the blood-vessels pierce the intestinal wall In true polyposis intestini, the polypi, which may be either sessile or pedunculated, preserve a smooth and rounded outline and are scattered evenly over the whole muc[illegible] the [illegible] hart-[illegible] disea[illegible] acqui[illegible] generations* This curious fact appears to have been recognized first in 1882 by Harrison Cripps, and it has since been commented upon by many writers

The disease is certainly more common in men than in women This fact was specially noted by Doering who, among his forty-two cases,

* See also Tønnesen's series

[illegible]



Fig. 84.—Polyposis intestini of the rectum.
(From a specimen in St Mark's Hospital, by permission of Dr Cuthbert Dukes)

are pedunculated, the elevation of the thickened mucosa resulting in the formation of a pedicle, but they may be sessile, and sometimes both varieties are found intermingled. Occasionally, one or more segments of the colon is specially affected, but as a rule the tumours are disseminated throughout its whole length. (Fig. 85)

In histological characters they are identical with the similar polypi found in the stomach and small intestine. The individual tumour has a basis derived from the fibrous tissue of the submucosa and is lined with cylindrical, deep-staining, goblet cells. Retention cysts are common.

Though many individual polypi retain their inflammatory character, there is a tendency to malignant changes. In fact, it is probable that, should the patient live long enough, carcinoma of the intestine is bound to supervene. Doering has reviewed the cause of death in thirty-six cases of polyposis and found that in twenty-one it was carcinoma; other fatal causes were intussusception, hæmorrhage, peritonitis and inanition. This tendency to carcinomatosis has undoubtedly given rise to the idea that carcinoma of the colon is hereditary.

By making serial sections of pedunculated polypi, Rankin, Bargen

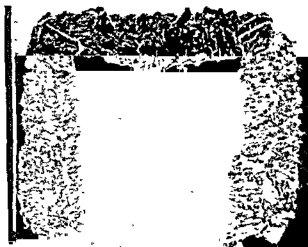


Fig. 85.—Polyposis of the large intestine of familial origin.
(From a specimen in St. Mark's Hospital, by permission of Sir C. Gordon-Watson.)

action is violent enough to cause actual avulsion of individual polypi and numerous cases of intussusception have been recorded from this cause.

Fonnesen, in a review of the microscopic pathology of all polypi described in the intestinal tract, divides them into three groups: those derived (a) from the epithelium, (b) from connective tissues, and (c) from the muscle layers. The first is by far the most frequent. In

the last two groups are fibroma, enchondroma, lipoma, myxoma, and sarcoma. The microscopic structure of individual growths in true polyposis suggests that they are adenomata with a special tendency to malignant changes

Symptoms.—The severity … great extent upon the area of … symptoms are abdominal pain … mucus stools. The diarrhœa varies in intensity, some patients having



Fig. 86.—Microscopic section of polyposis, showing early carcinomatous changes originating at the base. (*Author's case*)

but a mild looseness with two or three stools daily, others choleraic diarrhœa with thirty or more watery movements Usually diarrhœa alternates with constipation as in the true carcinomatosis. Occasionally nausea, vomiting, and anorexia are met with, and loss of weight and progressive weakness are usual In some cases large rectal hæmorrhages occur suddenly, this may be the first sign of the malady and causes a great change in the general appearance of the patient Occasionally polypoid masses are extruded from the anus

Pain ranges from indefinite abdominal distress to intermittent cramp and colicky pains, which may persist for days or even weeks In between attacks there is a sense of fullness over the whole colon, with vague discomfort which may be caused by increased tension

Intestinal obstruction occasionally occurs, and may be due to occlusion of the lumen by direct growth of the polypi, malignant changes in the

forms of rectal disease, or there may only be a sense of irritation Occasionally a large rectal hæmorrhage occurs

Diagnosis—In making a diagnosis, suggestive features are the absence of any ascertainable ætiological agent, the age of the patient (usually under thirty), and the familial character, if a history is obtainable

When the polypi are crowded into the rectum, as is usually the case, they may easily be felt by digital examination, but diagnosis is best made by proctoscopy or sigmoidoscopy The appearance of the polypi is characteristic Augier states that eighty to one hundred

instrument, and their microscopic structure ascertained

Infirmary

Radioscopic methods are of value X-rays after a barium enema, especially if applied by Fischer's double-contrast method, show most distinctly the presence and distribution of the polypi Fischer's

reached, whereupon successive stereoscopic pictures are taken

Polyposis is usually associated with secondary blood changes—

A farmer, aged thirty, entered hospital in February, 1933 He had come straight from Southern Rhodesia where he had been working for one year. There he was at first considered to be suffering from amœbic dysentery, for he

had attacks of diarrhœa with blood and mucus in the stools alternating with

similar excrescences On section the polypi were found to consist of typical adenomatous tissue, but at the base malignant cell nests had commenced to form (Fig 86) Later he was re-admitted for an exploratory operation but, when examined under an anæsthetic, masses were found by rectal and abdominal examination which showed that the malignant changes had already progressed and dissemination had already taken place The patient refused further operative procedure and died a month afterwards In his case no evidence of hereditary disposition could be obtained

The author has notes of four other cases, all in men, who were referred as suspected cases of intestinal amœbiasis; but none of them was as striking as the above, and in no others could the process of malignancy be so intimately observed

Duration of the disease.—*Polyposis is usually a long drawn-out, chronic, painful malady* In H Tønnesen's series of forty cases he recorded the duration as being under one year, six, one to five years, fourteen five to ten years, nine, ten to thirty years, eleven times. *The progress of the disease appears to bear no definite relation to the age of the patient*

Treatment.—Treatment of this very severe disease is undoubtedly unsatisfactory When it is limited to one segment of the bowel, resection of the involved area, or transperitoneal colectomy, *has been* performed When, however, the process involves the entire lumen of the bowel, colectomy is indicated, but this is a very formidable procedure, involving great risk Tonnesen has summarized the results of *total colectomy in a table giving the end results of operative measures.* Out of twenty-nine cases, twelve died In the remaining seventeen the results were excellent The primary operative mortality therefore stands at about 41 per cent, this including a case which died shortly *afterwards* (Table XVI)

As palliative measures, enterostomy, appendicostomy, colostomy, and ileostomy have all been advocated Ileostomy at least puts the colon at rest and may give relief, provided that malignant changes have not already set in

The results of radium therapy have so far been inconclusive. Bleeding from the bowel may be to some extent controlled by enemata of 1 per cent tannic acid or applications of Congo red as a hæmostatic

TABLE XVI

Authority	*Cases*	*Result*	*Period of observation*
Bardenhauser	1	dead	—
Borelius	1	good	10 years
Bratrud	1	good	1 year
Carrol	1	good	—
Coffey	3	1 good 2 dead	1½ years —
Czermade	1	dead	
Brentano	1	improved	—
Hauser	2	dead	—
Karajun	1	good	—
Lindner	1	good	4 years
Lilienthal	1	good	—
Lockhart Mummery	1	good	5 years
Morkowitz	1	good	—
Quenu	1	dead	—
Rotter	1	good	lived 2½ years
Riederer	1	good	died shortly afterwards
Schmieden	2	1 good 1 dead	—
Soper	1	good	—
Steinthal	1	good	—
Struthers	5	2 good 3 dead	6 years —
Sølling	1	dead	—

POLYPUS

Synonyms.—Simple adenoma, pedunculated adenoma

Ætiology—Polypus is the most common benign tumour of the rectum, and it is stated by F C Yeomans that two-thirds of all polypi of the intestinal tract occur in this locality It arises from the epithelium of the glands of the mucosa, generally in the lower and more easily accessible part of the rectum At first an adenoma is sessile, but owing to the constant traction set up on defæcation, it soon becomes pedunculated—so much so that polypi may be the exciting cause of local intussusception of the mucosa

According to A J Walton the term "polypus" denotes the actual configuration of the growth and refers to a pedunculated tumour whose microscopical appearance is that of an adenoma

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in chaplet form, as a ring encircling the bowel, and they tend to recur at the same site after surgical removal or cautery. Though usually situated within the rectal ampulla, large pedunculated polypi may protrude from the rectum

Lockhart-Mummery considers that the natural evolution of all rectal adenomata is to become eventually cancerous. From continued

The adenomata, however, may reach a large size without undergoing malignant changes

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polypus is attached to the bowel-wall by a long narrow pedicle, and is known as "soft rectal polypus." Sometimes it is branching and tree-like, and it is then known as a "villous tumour"; these usually exude a mucoid secretion often tinged with blood. When viewed through the proctoscope these polypi appear as delicate pink tendrils, ar

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with their presence When they are in the rectum, he complains of constant tenesmus, diarrhœa, and the intermittent passage of blood and mucus in the stools Often there is a smart and not inconsiderable hæmorrhage which, as in hæmorrhoids, may appear at the end of evacuation Children with polypi often scream with pain on passing stool, though they are free from symptoms at other times This alone should draw attention to the condition, and, in the absence of any constitutional symptoms, should serve as a signpost in the differential diagnosis from the dysenteries

Patients with polypi are usually full-blooded and of good complexion, and give the impression of being in good health.

Diagnosis.—The diagnosis of polypus is arrived at by a consideration of the history and course of the complaint, and by the presence of pain, discomfort, and tenesmus in a patient who is otherwise well Very often polypi can be palpated by a simple digital examination of the rectum, or, more satisfactorily, they can be visualized by the proctoscope or sigmoidoscope and their characters easily ascertained In case of doubt, a portion of the polyp should be removed by biopsy for microscopic examination. In every case a barium enema should be employed to reveal the possible existence of other polypi situated higher up the bowel

Some indication of the nature of the complaint may be obtained by a microscopic examination of the rectal discharge. In blood and mucus accompanying a polypus, there occur, usually, large numbers of

red blood-cells, and very often columnar epithelial cells, but there are no inflammatory pus-cells such as are visible in other irritative lesions The author has been able on several occasions to arrive at a diagnosis by these simple means

Treatment.—All polypi of the rectum should be removed as soon as possible. The older the patient the more likely are malignant changes to occur Small polypi and adenomata can be removed through a speculum or proctoscope, either being snared or snipped away with forceps, sometimes they can be ligatured When situated higher up in the rectum they can be twisted off by crocodile forceps, and the bases subsequently cauterized

Analysis of the Author's series of fourteen cases of adenomatous polypus of the rectum.

All these cases were originally referred as suffering from some kind of dysenteric disturbance, and the chief complaint was usually abdominal pain or the passage of blood and mucus, both or separately, in the fæces All the patients were males, their ages varying from five years to sixty seven, and all were tropical residents

The chief point of differentiation from dysentery was the benign character of the symptoms and the history of occasional passage of blood and mucus When blood was present in the fæces it was noted to be brighter in colour and more abundant than that usually found associated with amœbic dysentery Microscopic examination of these specimens shows comparative scarcity of pus and inflammatory cells and abundance of red blood cells An additional temptation to classify tropical cases as amœbic dysentery lay in the occasional presence of Charcot-Leyden crystals

In the majority of these cases, the polypi were multiple—in only two was a single polypus revealed—and situated 4 to 18 cm from the anus All proved on section to be benign adenomata

The following cases are cited as representative —

The first was that of a boy of six, who was sent from Northern Rhodesia as a case of incurable amœbic dysentery of 2½ years' duration There had been considerable hæmorrhage and he was anæmic as the result The diagnosis of probable polypus was made from a microscopic examination of the fæces A small polypus the size of a cherry was removed 10 cm from the anus

A man of twenty-nine from India had been treated off and on for eight years for presumed amœbic dysentery His chief symptoms were diarrhœa, and [illegible]

[illegible]

unquestioningly regarded as mucous colitis He described the mucus as

Lockhart-Mummery considers that the natural evolution of all rectal adenomata is to become eventually cancerous. From continued

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increased peristalsis When solitary polypi are situated high up in the colon, in the sigmoid, or beyond the range of the sigmoidoscope, it is obviously very difficult to associate the patient's variable symptoms with their presence. When they are in the rectum, he complains of constant tenesmus, diarrhœa, and the intermittent passage of blood and mucus in the stools Often there is a smart and not inconsiderable hæmorrhage which, as in hæmorrhoids, may appear at the end of evacuation Children with polypi often scream with pain on passing stool, though they are free from symptoms at other times This

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stools

passing in strings and masses and leaking through the anus, sometimes, eight to twenty times a day. Directly he took any form of exercise the discharge



P. H. M.-B.

Fig. 87.—Adenomatous polypi removed from the rectum. The mass resembles a cauliflower in shape and appearance. (*Half nat. size.*)

polypus, 3' inches in diameter, was removed at operation by T. P. Kilner. (Fig. 87.) On section it proved to be a simple adenoma. There was a small recurrence at the site four years later, which was also removed. The patient's general health has since remained excellent.

The main interest of this case was the resemblance to mucous colitis, the absence of blood in the fæces, and the benign nature of the symptoms produced, in view of the size of the tumour.

CHAPTER XXVIII

ACTINOMYCOSIS, TUBERCULOSIS AND SYPHILIS OF THE LARGE INTESTINE

ACTINOMYCOSIS OF THE LARGE INTESTINE

ACTINOMYCOSIS is an infection by a fungus of the genus Actinomyces (*Streptothrix actinomyces*) It is characterized by a tendency to form abscesses, sinuses, and granulation tissue, often it invades the surrounding tissue

Actinomycosis of the large intestine is probably more prevalent than is usually believed It commonly commences in the ileo-cæcal region, and it is clear that the point of origin is a diseased appendix It is well known that ruptured appendices may heal up and leave little trace behind, and thus, actinomycosis spores may escape into the abdominal cavity When the actinomycoma commences to grow, it is always subperitoneal and advances upwards inexorably The hard swellings sooner or later soften and the semi-fluid material finds its way to the surface of the body and produces red fluctuating areas From these abscesses actinomycotic pus may be obtained In the transverse colon the lesions tend to develop external to the gut rather than in the gut-wall and are apt to be mistaken for carcinoma

Secondary rectal actinomycosis is the form in which the primary focus of the disease is in some other viscus, whence it extends to the rectum Primary rectal actinomycosis presents a more definite picture Infection takes place high up in the rectal canal and spreads in the loose, cellular tissue towards the iliac fossa and hypogastrium Z Cope (1938) has described the sigmoidoscopic appearances of a case under the care of Gordon-Taylor There is irregularity and puckering, which is somewhat comparable to that observed in skin lesions, and a few yellow submucous actinomycotic granules are visible In the case described there was stenosis of the rectum 4 cm from the anal orifice Actinomycosis of the stomach and small intestine are pathological curiosities

Pathology —When the fungi occur in colonies, they form masses which are visible to the naked eye, having a yellowish, or sulphur-like appearance, in each colony there are rays, like a group of clubs, which emanate from a central mass There is some evidence that the infecting fungus is derived from a carious tooth, or it may be from the tonsils In the mouth the disease often develops after extraction of teeth

Actinomycosis is a most destructive disease, and in animals it pene-

trates the interstices of bones with the same ease with which it invades muscles

Symptoms.—In abdominal actinomycosis, acute, chronic, and pyæmic forms occur. The chronic form is the only one which can be diagnosed with certainty, but the distinction from malignant disease and tuberculosis is extremely difficult, and becomes increasingly so until sinuses are formed, which discharge the characteristic sanious pus containing sulphur granules It is from these granules that the ray

systemic pyæmia has been described by N H. Fairley and F. P. Mackie

This patient, who came from China, was in hospital in December, 1934 The irregular fever with rigors, associated with night sweats and an enlarged liver, suggested at first hepatic abscess, a dense opacity in the liver area *(shown by X-rays) supporting this diagnosis An exploratory laparotomy was* performed, and subsequently the patient died. At autopsy numerous necrotic and suppurating areas were found in the liver. The sigmoid flexure and the descending colon were matted together by adhesions, and punched-out

An almost identical case is described by Rankin, Bargen, and Buie In this case appendicitis was first diagnosed; and the appendix was removed. Subsequently, symptoms suggestive of hepatic abscess *supervened* Actinomycotic disease of the large intestines may be associated with chronic diarrhœa and occasionally with dysentery-like stools

Diagnosis.—Diagnosis is established by finding the yellowish-green sulphur granules in which, when crushed on a glass slide, the characteristic clubs may be recognized. They may be confused with inspissated pus.

Chronic tumefaction due to actinomycosis, unaccompanied by the formation of sinuses, may be confused primarily with hyperplastic

given in massive doses. The first success was reported by O Walker (1938); others by E M Miller and E. H Fell (1939), W H Ogilvie, G C. Dorling and N. L Eckhoff (1940) The latter treated five severe abdominal infections, four recovered completely and one died. In one case later operation showed that all evidence of the disease had disappeared Sulphapyridine appears the drug of choice, in doses of 6 grm, daily for four days—a total of 24 grm —succeeded later by a course of 38 grm E. M Miller and E H Fell's case was in a boy of 11 who had 1 9 grm for seven days and subsequently increased in weight 100 lbs. in one and a half years

The success of bowel resection in actinomycosis depends on the possibility of completely removing the infected portions

TUBERCULOSIS OF THE LARGE INTESTINE

It is generally held that tuberculous infection of the colon is rare as compared with the incidence of this disease in the small intestine. Amongst 230 adult patients who died of tuberculosis, Goldberg and Smithies found intestinal tuberculous lesions in over 80 per cent In 1911 Park and Krumweide, reviewing fifty-five cases of abdominal tuberculosis, found that in children under five years of age, the bovine type of bacillus was responsible for the infection in 59 per cent of cases; in those ranging from five to sixteen years of age, it was the causative agent in 46 per cent, but in patients of sixteen years, or over, it accounted for only 22 per cent It therefore appears that the human type of bacillus is the chief factor in the intestinal tuberculosis of adults

Intestinal tuberculosis is a disease of relatively young people Thus, Brown and Gaither found the average age to be about thirty-five

been diagnosed as actinomycosis, sarcoma, and even carcinoma

In recent years medical interest has centred upon the hyperplastic form of tuberculosis, which mainly affects the cæcum and tends to

patient than of the large numbers of bacilli ingested

The terminal ileum and cæcum are the portions most usually at-

secondary to pulmonary lesions

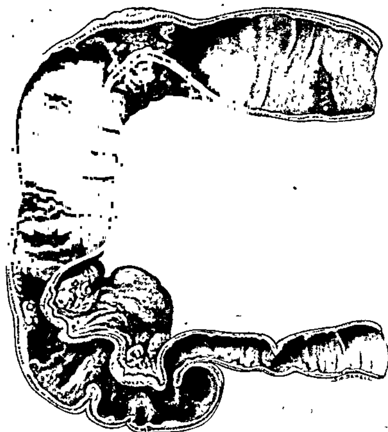


Fig 88.—Tuberculosis of cæcum and ascending colon, showing hypertrophic type of lesion and several shallow girdle ulcers.
(*By permission of Sir C Gordon-Watson*)

Previous damage to the intestinal mucosa from dysenteric infection definitely predisposes to tuberculous disease, this is probably the reason for the relative frequency of primary tuberculous infection of the large intestine in tropical practice

Pathology.—In the ulcerative type of lesion, which is the one

The tuberculous ulcers possess certain characteristics which render their recognition relatively easy They occur at right angles to the long axis of the bowel, and have a tendency to become annular in shape. As a rule, the more recent ulcers have diffusely caseous bases

[illegible]

omentum and parietal peritoneum are commonly encountered Rarely, pseudo-polyposis resembling that of ulcerative colitis is produced (A L Taylor, Bristol General Hospital)

In the *hyperplastic* type of tuberculosis the process may extend along the intestine for varying distances, but is usually confined to one segment The tumour produced is hard, dense and usually red The tubercle bacilli infiltrating the bowel-wall produce fibrous hyperplasia rather than the caseation encountered in the ulcerative form The bacilli are very sparsely distributed, being demonstrated with difficulty

Gross or hyperplastic tuberculosis of the rectum consists of massive involvement of part or even the whole of the rectal canal the wall of [illegible]

infection

Ulcerative type. *Symptoms*—It is necessary, especially in the ulcerative type, that the disease should be recognized early, in order that appropriate treatment may be instituted as soon as possible In persons who are known to have tuberculosis, recognition is comparatively easy It must, of course, be borne in mind that diarrhœa occurs quite commonly in advanced pulmonary tuberculosis, without any recognizable intestinal lesion It may alternate with constipation During an attack of diarrhœa, the stools are usually profuse, thin, watery, and very offensive, while blood, though not obvious, can [illegible]

[illegible] ulcerative tuberculosis undoubtedly do occur in which, on account of the accompanying pyrexia, the distress of the patient, the exhaustion and toxæmia and, mainly, the blood-and-mucus discharges, idiopathic ulcerative colitis is mimicked very closely

[illegible]

appear as an elastic cord. Enlarged mesenteric glands may be palpable On the other hand, in the author's series of cases the majority presented no physical signs in the abdomen at all

Diagnosis.—At the outset it can be stated that there is no single clinical

proctoscopy or sigmoidoscopy. This is by no means always easy.

There are cases in which the acid-fast bacilli are so numerous in the discharges that their recognition is a simple matter in ordinary fixed-smear preparations of the fæces. There are others again in which the *organisms are so scanty that they can be demonstrated solely by concentration methods.* The demonstration of acid- and alcohol-fast organisms in the fæces in a case which is suspicious from the clinical aspect may be taken as a further indication that the case is tuberculous in origin. It is, however, not quite such an easy matter to decide whether *all* acid-fast bacilli in the fæces are necessarily tubercle bacilli. (*See* p. 569.)

Proctoscopic examinations should always be undertaken in intestinal ulcerative tuberculosis; but it is admittedly extremely difficult to make a diagnosis in every case by this examination alone. Where ulcers can be visualized, they must be scraped and microscopical preparations made; a positive diagnosis can then be made by demonstration of acid-fast bacilli in the lesions. The ulcers are fairly distinctive in appearance, with undermined pearly edges and grey bases. In patients who have recognized pulmonary tuberculosis the existence

culous ulcers closely resemble those produced by *Entamoeba histolytica.*

Tuberculosis of the ulcerative type has also to be differentiated *from the many different forms of dysentery and colitis.*

Hyperplastic form. *Symptoms.*—The hyperplastic form is more difficult to recognize in the early stages than is the ulcerative type. *The problem is complicated by the fact that gross lesions of the cæcum* and other parts of the colon may be present for long periods without producing symptoms. Pain is by no means constant and varies in

the clinical picture.

Diagnosis.—The diagnosis of cæcal tuberculosis is often made through the accidental discovery of a tumour unaccompanied by any

severe or localizing symptoms (Table XVII, p 522) Its recognition has, however, been greaty facilitated by the method of J Gershon-Cohen who has employed the double-contrast method of successive injections of barium, succeeded by inflation with air

Removal of a piece of tissue for microscopic examination should always be undertaken, but though it may have giant cells and present the pathological picture of tuberculosis, the demonstration of tubercle bacilli is inconstant

Differential diagnosis from carcinoma, or from diverticulitis, is by no means easy, but as a general rule, tuberculosis progresses more slowly and insiduously and affects younger people Examination of the blood may here be of some value, the anæmia in patients with tuberculosis of the cæcum being less severe than those with carcinomatous involvement of the same region The blood sedimentation rate may be of value

The picture of acute anæmia synchronously with tumefaction in the right iliac fossa is more characteristic of carcinoma of the cæcum than of any other condition

Hyperplastic tuberculosis has also to be distinguished from chronic

tuberculosis give the Stierlin sign, that is, show hyper-irritability and hyper-motility, especially of the cæcum, with lack of haustral segmentation and irregularity of contour; but this sign is not of absolute diagnostic value, as any type of ulceration of the colon may produce the same appearances

Complications.—The main complications of tuberculosis of the bowel are stricture, perforation, and hæmorrhage Actual stenosis and stricture in tuberculous disease progress slowly. When a fluctuating tender mass, usually on the right side of the abdomen, in the

given good results, and deep X-ray therapy has been advocated by some workers Of drugs, cod-liver oil, halibut-liver oil and similar preparations are indicated. Calcium and parathyroid therapy have found favour

Hyperplastic tuberculosis demands surgical intervention, and three

surgical procedures have been especially advocated: enterostomy, short-circuiting, and total resection of the loop of bowel involved

Tuberculous peritonitis, both of the ascitic and plastic types, may be *associated with chronic diarrhœa, especially when tubercular* ulceration of the bowel is present in addition.

The following illustrative cases may be cited:—

1 Tuberculous ulceration of the large intestine, resembling chronic bacillary dysentery and, in radiological appearances, ulcerative colitis.

A married woman of twenty-seven was first seen in December, 1933, when she was complaining of prolonged diarrhœa with the passage of dysenteric stools and occasionally blood These dysenteric symptoms had persisted for 2½ years, after residence in Ceylon, and had led to a diagnosis of amœbic and later of bacillary dysentery. The stools contained pus, blood, and macrophage cells The white blood-count was 7,000 and the lymphocytes numbered 21 per cent. Tuberculous ulceration of the rectum was demonstrated *by sigmoidoscopy, and typical acid fast bacilli were obtained from* preparations made from the ulcers (Plate XIX, F, facing p 450) In an

years later. There was no evidence of any tuberculous focus in the lungs.

2. A man of fifty-six was first seen in October, 1935, complaining of diarrhœa and dysenteric symptoms together with a loss of 28 lb in weight The stools, which were liquid and extremely offensive, contained pus and *macrophage cells By the antiformin method of concentration*, acid fast bacilli were demonstrated Here again, the picture obtained by barium enema was one of chronic colitis, giving the typical smooth appearance and lack of haustration A bunch of calcareous retrocæcal glands was also visualized. The sigmoidoscopic picture was that of a granular colitis Although improvement was obtained by a month in hospital, with gain in weight of 14 lb, the prognosis was unfavourable.

Valvular cæcostomy was performed in December, 1921, and was apparently successful, but the patient died a year later from streptococcal septicæmia, the infection originating in the cæcostomy wound. At autopsy, stenosis, sacculation, and tuberculous ulceration of the large intestine were demonstrated, *the microscopic sections showing the typical histological picture of* tuberculosis (Fig 89)

4. A girl of 8½ came from Durban, South Africa, where she had been

suffering from "dysentery," with blood and mucus in the stools, for the past two years At first she was regarded as an intractable case of amœbic dysentery and was treated accordingly, without benefit On arrival in England in September, 1933, the child was very emaciated, with oedema of



Fig 89—Microscopic section of ascending colon, showing tuberculous injection of the longitudinal muscularis layer

Her appearance suggested tuberculosis There was a hectic flush on the cheeks, a hectic temperature, fine down on the face, and lanugo hairs on the body Moreover, an X-ray of the abdomen showed calcareous retrocæcal glands The differential blood-count was also suggestive, the proportion of lymphocytes being as high as 64 per cent The diagnosis was completely established when masses of acid fast bacilli were demonstrated in blood and mucus passed per rectum subsequent to continuous lavage through the

The barium enema also showed the smooth surface and lack of haustration so characteristic of this disease The vicarious appearance of tubercle bacilli in the fæces is also to be noted

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3 In November, 1921, the case of a laboratory assistant aged twenty-five was investigated. There appeared to be a war infection which commenced in Salonica in 1917, and had been diagnosed and treated as amœbic dysentery. The patient was ill and emaciated The numerous stools contained blood,

Valvular cæcostomy was performed in December, 1921, and was apparently

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tuberculosis.

4. A girl of 8½ came from Durban, South Africa, where she had been

however, the resolution of the lesions on the institution of antisyphilitic treatment

The radioscopic appearances of extensive syphilitic stricture of the rectum have been described by C. J Drueck There is no ampulla, only a smooth general contracture of the lumen, beginning above the internal sphincter. The stricture is usually long and pencil like, and the opening into it may be funnel-shaped

Treatment.—This consists of the usual antisyphilitic treatment, vigorously prosecuted The actual cautery may perhaps have to be employed for excision and cauterization of the condylomata When stenosis is present, operative measures, such as short-circuiting or colostomy, may be required.

SYPHILIS OF COLON AND RECTUM

It was formerly thought that syphilitic ulceration and syphilitic disease of the large intestine were of great moment, but the attitude

important factor in rectal strictures as a whole.

There are two types of syphilis of the large intestine: a primary

considered further

Among the later lesions of intestinal syphilis is the gummatous colitis described by R. Maingot The gummata may be single or multiple, they may start as small nodules which grow relatively rapidly, so that in the course of a few months they measure about 5 cm in diameter Later, they ulcerate and a mixed bloodstained exudate escapes, which may give rise to blood-and-mucus discharges in the stool *Eventually a tubular stenosis of the rectum forms and* may lead to obstruction, though not to actual fibrous stricture. Of this form of syphilitic colitis the author has encountered only one case in his series

This was in a ship's steward seen in *1925*. A definite history of syphilis of four years' duration was given, and the Wassermann reaction was strongly positive The case was complicated by extensive peri-anal ulceration and suppuration of glands in both groins, suggesting lymphogranuloma inguinale. The fæces contained blood and mucus Two definite rectal strictures and a

G M Gray has reported two cases from Nigeria which were cured by antisyphilitic treatment (Lockhart-Mummery). The best description is given by Charters Symonds (1922), who describes it as

positive serological tests for *syphilis. The most telling method is,*

pigs produces an inguinal bubo in every case, this method can therefore be employed for diagnosis The most reliable test at present in use (Findlay) is, however, the intracerebral inoculation of white mice, which produces an encephalitis The serum of an infected person contains antibodies, hence a protection test has been devised by mixing equal parts of the serum from a bubo patient with an emulsion of mouse-brain diluted 1 5 in normal saline, and kept for twelve hours in an ice-box at 4° C When injected in doses of 0 5 c c intracerebrally, no reaction is produced

Recently Y Miyagawa (1936) has found in Japan that a squirrel (*Entamias asiaticus orientalis*) is highly susceptible to intratesticular and intracerebral inoculation He has, moreover, been able to cultivate the virus in chorio-allantoic membrane of the chick embryo in tissue culture

Ravaut, Levaditi, Lambling and Cachera, finding that they were unable to inoculate monkeys intracerebrally with contaminated material from the rectum, devised a method of inoculating a portion of tissue removed from a case of ulcerative proctitis under the skin of a guinea-pig After a few days the inguinal lymphatic gland was excised,

granuloma, a small herpetiform vesicle, or ulcer, on the prepuce, which heals up in a few days From this point the virus travels *via* the lymphatics to the inguinal glands The incubation period, before the

implicated

The affected glands gradually enlarge, and after a period of several weeks—or even months—the swellings break down and suppurate. Sometimes they subside without suppuration and are hard and extremely tender Fistulous tracks may form, from which a serous and sticky fluid exudes If much lymphatic tissue is removed by operation, an elephantoid condition of the scrotum and leg may ensue.

Climatic buboes in the groin have definite physical characteristics which serve to distinguish them from other suppurative lesions, such as septic buboes, plague and filariasis Sometimes painful effusions, probably due to toxic absorption, are noted in the larger joints. Extragenital infections have been recorded—on the tongue, followed by glandular enlargements in the neck (W Curth), in the axilla (S. Hellerström), and on the foot (Lepinez and Grévin) The author has also seen the cervical glands affected in an Indian seaman with inguinal buboes

CHAPTER XXIX

LYMPHOGRANULOMA AND CHRONIC CICATRIZING ENTERITIS (CROHN'S DISEASE)

LYMPHOGRANULOMA INGUINALE
(Genito-ano-rectal syndrome)

Synonyms.—Climatic Bubo Inguinal Poradenitis Nicolas-Favre Disease

Definition.—Lymphogranuloma inguinale is now known to be due to a filterable virus which, entering through a small primary vesicle and travelling *via* the lymphatics, causes inflammation and suppuration of the inguinal glands At this stage it can cause constitutional disturbances, such as pyrexia, in severe degree.

In the male, buboes are produced in the groin, sometimes in the axilla and neck , in the female they are rarely seen, but there occurs a general lymphœdema of the vagina and labia, known as "esthiomène." In both sexes infiltration of the perirectal tissues takes place, resulting in ulceration and stricture, known as the genito-ano-rectal syndrome It is with the rectal aspects of lymphogranuloma that this account is mainly concerned

Knowledge on this subject is comparatively recent.

Ætiology.—The bubo termed "climatic bubo" is well known in tropical practice ; it is especially prevalent among Europeans in West Africa, India, China, Malaya, Japan, the southern Mediterranean, the West Indies, and South America In France F. M Durand, J. Nicolas, and M Favre (1913) described this condition, as "Lymphogranuloma inguinale," and it has been realized that the virus is widespread in France and Germany, and indeed throughout the whole of Europe Since 1933 several cases have been reported in England. The writer had one case (1935) in a woman from Soho, London, whose husband was similarly affected In the United States this disease has been *recognized in all its manifestations, especially among the negro* population.

The virus.—In 1930 S Hellerström and E. Wassén transmitted the virus obtained from the pus of inguinal buboes to monkeys , intracerebral inoculation produced a meningo-encephalitis. An emulsion prepared from the cerebral tissues produced, on intradermal injection, *a local manifestation known as the Frei-Hoffmann reaction* The virus of lymphogranuloma belongs to the filterable group, and it has been shown by G. M Findlay (1932) that intraglandular injection of guinea-

this method can therefore ble test at present in use ioculation of white mice, im of an infected person

reaction is produced

Recently Y Miyagawa (1936) has found in Japan that a squirrel (*Entamias asiaticus orientalis*) is highly susceptible to intratesticular and intracerebral inoculation He has, moreover, been able to cultivate the virus in chorio-allantoic membrane of the chick embryo in tissue culture

Ravaut, Levaditi, Lambling and Cachera, finding that they were unable to inoculate monkeys intracerebrally with contaminated mater-

Symptoms

H M Hanschell (1926) described, as the primary lesion of lymphogranuloma, a small herpetiform vesicle, or ulcer, on the prepuce, which heals up in a few days From this point the virus travels *via* the lymphatics to the inguinal glands The incubation period, before the

Usually, in well-marked cases, the internal iliac glands are also implicated

The affected glands gradually enlarge, and after a period of several weeks—or even months—the swellings break down and suppurate. Sometimes they subside without suppuration and are hard and extremely tender Fistulous tracks may form, from which a serous and sticky fluid exudes If much lymphatic tissue is removed by

buboes

Patients with rectal lymphadenoma usually present the symptoms of stricture, and pass malformed or ribbon-shaped fæces. Tenesmus, intestinal colic, and alternating diarrhœa and constipation are common. *Usually there are associated rectal fistulæ.*

Rectal lesions.—Nearly all authorities are now agreed that non-malignant strictures of the rectum, in both sexes, are generally not syphilitic in origin but are due to the virus of lymphogranuloma. In 1932, Frei and Koppel applied the intradermal test in cases of rectal stricture where syphilis could be excluded, and obtained a positive result. O. Jersild (1930) originally suggested the term genito-ano-rectal syndrome for the symptom-complex seen in women who present the combination of esthiomène (vulval elephantiasis) with rectal stricture. In 1930 the same investigator reported upon twenty-three cases, in all of which the intradermal test was positive. Since then, results have been confirmed by French workers. W. Frei (1932) reported that 80 per cent. of cases presenting the genito-ano-rectal syndrome have given positive intradermal tests. Bensaude and Lambling in Paris (1931) found 86.6 per cent. of strictures and 92.5 per cent. of proctitis cases to be Frei-positive. They recorded twenty-one cases of anal stricture in women; in twelve of the fourteen cases manifesting no other lesion, Frei's intradermal test was positive. In the United States, H. P. de Wolf and J. V. Van Cleve found, among 1,010 cases subjected to the intradermal test, fifty-eight positive reactions, of which fifty-five were cases of lymphogranuloma and three had ano-rectal disease.

The sexual incidence of rectal strictures has been remarked upon by nearly every observer; it is very much more frequent in the female than the male, the proportions being about six to one. In India, however, the proportions appear to be reversed. Rajam, in a review of 183 cases in Madras, reports rectal strictures in 18 male and 8 female patients.

It is now generally recognized from the work of Bensaude and

The position of the stricture has been noted by many surgeons. Perret, in fifty-six cases, gives its situation as follows: At the anus, in four; less than 6 cm. above the anus, in thirty-two; between 6 and 9 cm. of anus, in fourteen; in the colon, in six. R. Barthels and H. Biberstein believe that in the majority of cases the stricture lies from 2 cm. to 6 cm. above the anus. The association of vulval and ano-rectal lesions has been recognized by many workers.

... according to their dura-
... morido-
... nd also
... nuloma

virus to the production of the genito-ano-rectal syndrome appears to be as follows:—

In the female, if the initial sore occurs in the upper two-thirds of the vulva, the virus will, in a great proportion of cases, pass to the inguinal glands and, as in the male, an inguinal bubo will result. If, on the other hand, the lesion is situated towards the posterior part of the vulva or in the vagina, then the infection will pass to the intra-pelvic glands and lymph plexuses which drain the lower part of the rectum, and a retrograde lymphangitis takes place In the walls of the rectum the maximal incidence occurs between 2 and 6 cm above the anus—that is at the lower border of the ampulla just below its upper margin—at the situation where strictures are most common

T R Peyton, in his classification of rectal strictures due to this virus, finds that it at first produces proctitis, then, especially in women, is associated with esthiomène and anal stricture later, annular and tubular rectal strictures, and finally, rectal communicating strictures from ulceration between rectum bladder, vagina, prostate and seminal vesicles

Rectal stricture due to the virus of lymphogranuloma must be rare, at least in England From an analysis from 3,068 sigmoidoscopic examinations made during fifteen years, in the Hospital for Tropical Diseases, there were only two cases of rectal stricture giving a Frei-Hoffmann reaction The particulars of these two cases are given below

The first was seen in 1934 in a man aged sixty who had a hard rectal stricture 3 cm from the anus, below the stricture the surface was ulcerated and there were numerous fistulæ The intradermal Frei-Hoffmann reaction performed with Findlay's antigen was positive It appears that twenty two years previously, in China, the patient had contracted lympho-

stricture with dilatation resulted in great improvement

The second case, in a male patient from South America, came under the care of N H Fairley in July, 1935 The patient gave a history of rectal trouble following climatic bubo and extending over a period of nine years, with fistula formation and a muco purulent discharge from the rectum Although he had acquired syphilis many years previously, the Wassermann reaction both in the blood and cerebro spinal fluid was negative There was also a history of several attacks of gonorrhœa including a gonorrhœal proctitis In 1926 he had climat...

9 cm. from the anus Histological examination of a small portion revealed

no carcinomatous changes. During instrumentation a copious discharge of fluid pus took place from a peri-anal sinus.

The importance of the following case to British practitioners is self-evident.

A fatal and extremely advanced and undiagnosed case was seen in July, 1941, in a woman of forty five. Undoubtedly the original infection had been contracted in England in 1920. Two years after marriage she began to suffer from rectal ulceration which was thought to be "piles." Since that time, for a period of eighteen years, constipation had been acute and pararectal fistulæ had appeared Gradually, signs of subacute obstruction became more



Fig. 90.—Lymphogranuloma inguinale: stricture of the rectum with fistulæ and ano-genital elephantiasis.
(After R. Bensaude and A. Lambling)

died shortly afterwards from intestinal obstruction

Ocular complications have been described by J A Macnie (1941) These consist of uveitis and kerato-conjunctivitis Sometimes the whole globe is covered with granulomata, and monkeys have been infected with extracts of this material The Frei-Hoffmann reaction is positive

W Curth and his associates (1940) have also isolated the lymphogranuloma virus from three cases of chronic granulomatous conjunctivitis with secondary pannus, by tissue culture and animal inoculation (mouse and monkey) The former method was found more practicable Treatment with sulphanilamide was effective in stopping the active process

Diagnosis.—The symptoms produced by this syndrome are mostly those of rectal stricture with intermittent attacks of diarrhœa The clinical diagnosis is made in the first place by digital examination of the rectum A hard fibrous and annular rectal stricture certainly suggests this condition Sometimes the indurated mucous membrane imparts a nodular, warty sensation to the examining finger (Fig 90)

The diagnosis is confirmed by the intracuti reaction (intradermal test) which is now known as the Frei-Hoffmann reaction The antigen is prepared from the diseased gland tissue, or from pus from the buboes Pus is withdrawn from a gland which has undergone softening but not fistulation, and is mixed with physiological saline in a sterile tube in the proportion of one part to five Thus prepared, it is heated to 60° C for two hours over a water bath, and the following day to 60° C. for one hour The antigen is preserved at a low temperature unexposed to light. Tests must be repeated every three months and should give *negative* reactions in the skin of normal and control patients.

Other sources of antigen consist of emulsified glands and, more recently, of similarly prepared mouse brains infected with this virus Some doubt exists on the score of pseudo-reactions caused by normal brain tissue Better results have been obtained by S E Sulkin (1941) and collaborators by employing *Lygranum*, prepared directly from [illegible] has drawn up minute [illegible] it must be protected [illegible] ible temperature—the [illegible] its efficacy. The test [illegible] he Dick sensitization test, 0 1 c c. of the antigen being administered intracutaneously in the forearm, where it causes a wheal 9 to 10 mm in diameter A positive result usually appears between twenty-four and forty-eight hours after

no carcinomatous changes. During instrumentation a copious discharge of fluid pus took place from a peri-anal sinus.

The importance of the following case to British practitioners is self-evident

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for a period of eighteen years, constipation had been acute and pararectal fistulæ had appeared Gradually, signs of subacute obstruction became more



Fig. 90.—Lymphogranuloma inguinale: stricture of the rectum with fistulæ and ano-genital elephantiasis.
(After R. Bensaude and A. Lambling)

being tuberculous in origin, but no subserous tubercles have ever been observed

That the disease is progressive is shown by the fact that in some patients who have undergone resection of the ileo-cæcal portion of the intestinal tract, the disease has spread into the proximal portion of the ileum No light has so far been shed upon the nature of the virus which may give rise to this chronic inflammation Likely and Lisa (1939) have suggested that it may be allied to that of lymphogranuloma



Fig. 92.—Microscopic section of lower ileum in chronic cicatrizing enteritis (Crohn's disease), showing fibrosis, mainly of the submucosa, and giant cells with included crystalline bodies. The circular muscular coat is also affected. (*Author's case*)

inguinale They found at autopsy multiple granulomata of the ileum in a negress with the genito-ano rectal syndrome

Pathology.—The pathological condition consists of a fibroblastic reaction with an infiltration of polymorphonuclear leucocytes, and round or plasma cells The mucous membrane of the parts affected is ulcerated and the submucosa much thickened by cellular infiltration A striking feature is the presence of giant cells of the foreign-body type

walls, with encroachment on the lumen.

CHRONIC CICATRIZING ENTERITIS

Synonyms.—Regional Ileitis; Crohn's Disease

This rare disease is included in this work in order to draw more general attention to the condition and to emphasize the possible necessity of differentiating it from other forms of

the colon are of the same nature.

History.—The importance of benign, non-specific granulomata

Almost all the recorded cases of this condition are to be found in American literature; only a few instances have been found in Great Britain. In 1933 Molesworth reported a single case with stenosis of the ileo-cæcal valve, and in 1934 Jackman described two cases as localized hypertrophic enteritis. In 1935 Dickson Wright exhibited two more at the Medical Society of London. In 1936 Barbour and Stokes gave an excellent synopsis of regional ileitis, together with a completely worked-out account of an autopsy on a mental patient. This patient had also been investigated by the author at one stage of his illness. P. W. Brown, J. A. Bargen, and H. M. Weber (1934) have

noteworthy. Crohn originally described the condition as chiefly affecting young adolescents, but cases have since been reported involving all ages. The age of the case reported by R. F. Barbour and A B Stokes was sixty-three.

Ætiology.—The ileum, the jejunum, and small portions of the cæcum may be involved. It is now recognized that the large intestine is also quite commonly affected. T. G. James describes a case in which the large bowel, from the distal part of the transverse to the pelvic colon, was implicated The descriptions of regional ileitis by surgeons who have performed exploratory operations are all strikingly similar There is an inflammatory process, sharply localized in area, involving all layers of the intestinal wall and associated with hypertrophy, the whole mass simulating in rigidity and appearance a stiff rubber tube. Naturally, this fibrotic thickening has been suspected of

the involved portion with destruction of the mucosa. A radiographic examination demands close scrutiny of each individual segment by observing the descending opaque meal Careful investigation of the terminal portion of the ileum, after it has been distended as the opaque enema passes through the ileo-cæcal orifice, is also necessary Kantor says that in the extreme narrowing of the terminal ileum the "string sign" is produced A W Galambos and W Mittelman, J. L Kantor, H M Weber, and others all believe the X-ray appearances to be typical and diagnostic when the terminal ileum is involved Sigmoidoscopy is usually of little avail in arriving at a diagnosis

The differential diagnosis has to be made from malignant disease, diverticulitis, hyperplastic tuberculosis, lymphadenoma, actinomycosis, and syphilis, the localized inflammatory masses must be distinguished from chronic appendicitis, Meckel's diverticulum, chronic intussusception, and twisted ovarian cyst Cases with diarrhœa have to be differentiated from the various types of colitis, especially ulcerative colitis, and dysentery.

Treatment.—The treatment of Crohn's disease is generally admitted to be a surgical problem The main possibilities are to short-circuit the lesion, to resect it, or to short circuit it first and resect later C G Mixter prefers resection but admits that the mortality is high The disease cannot be treated with any degree of success by medical means

B B Crohn (1939) emphasizes once more the necessity of early [illegible]

[illegible]

loops of intestine was performed in 22 patients without a fatality [illegible]

[illegible]

A M Snell (private communication) has made the interesting and pregnant observation that the sprue syndrome may supervene after removal of recurring cicatrizations of the jejunum and upper ileum

Every effort which has been made by different investigators to demonstrate tubercle bacilli (mainly by the injection of material into

the formation of giant cell systems, which are also present in the regional mesenteric glands Viewed as a whole, the histological picture cannot be distinguished from that of tuberculosis. Ulceration and fistulæ are secondary to the primary lesion

Symptoms.—An almost constant complaint is pain which, when the disease is confined to the jejunum, is apparently localized to the umbilicus; when the cæcum and ascending colon are involved, together with the ileum, the pain is in the upper portion of the abdomen. Diarrhœa is almost invariable, and the information so far obtained suggests that its presence or absence is in some way connected with the situation of the lesions and the extent of the pathological changes Usually the stools are loose and watery without much urgency and without visible blood Vomiting is an important symptom Most of the patients have bouts of pyrexia and generally there is loss of weight Intestinal fistulæ occurred twice in eighteen cases in Brown, Bargen and Weber's series. There is usually a mild secondary anæmia and a mild leucocytosis of 10,000

Crohn divided his cases into four clinical types, a classification which has since been accepted :—

1. Acute intra-abdominal disease with peritoneal irritation.
2. Ulcerative enteritis.
3. Chronic obstruction of the small intestine.
4. Persistent intractable fistulæ in the right lower quadrant.

In the first type appendicitis may be simulated ; in the second the

impossible Sometimes, even, it is only after resection that tubercle and carcinoma can be excluded.

The X-ray appearances of the inflammatory processes in the small intestine and in the large are practically the same. There is mural thickening with consequent stenosis, and stiffening and shortening of

e involved portion with destruction of the mucosa A radiographic amination demands close scrutiny of each individual segment by serving the descending opaque meal Careful investigation of the rminal portion of the ileum, after it has been distended as the opaque nema passes through the ileo-cæcal orifice, is also necessary Kantor ys that in the extreme narrowing of the terminal ileum the "string gn" is produced A W Galambos and W Mittelman, J L Kantor,

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[illegible]

A M Snell (private communication) has made the interesting and pregnant observation that the sprue syndrome may supervene after removal of recurring cicatrizations of the jejunum and upper ileum.

CHAPTER XXX

DIVERTICULITIS, INTUSSUSCEPTION, HÆMORRHOIDS, FOREIGN BODIES IN THE RECTUM

DIVERTICULITIS AND DIVERTICULOSIS

It is beyond the scope of the present work to describe in detail the large amount of research which has been devoted to this subject in recent years. The conditions will be dealt with only in so far as they

Fæcoliths which form in the the lumen of the colon, but flammation or *diverticulitis*.

were present in 10 per cent. From autopsy records of 1,925 cases (1924–28), Rankin and Brown at the Mayo Clinic found diverticula in 5 2 per cent It is probably a fair estimate that the incidence of diverticulosis in those over forty is about 5 per cent and in only some 17 per cent of these are symptoms of diverticulitis present

H. C Edwards found that the youngest in his series of cases was

point, but recent observers are by no means in agreement that this is

the true explanation H C Edwards points out that the circumference of the intestine through which diverticula emerge is governed by two anatomical factors the disposition of the longitudinal muscle-fibres and the mode of entry of the blood-vessels The sites of election for the formation of diverticula are arranged in two rows immediately to the mesenteric side of the two lateral muscular tæniæ Each diverticulum starts by the migration of a wedge-shaped process of mucous membrane through the circular muscle-fibres at the point of entry of a blood-vessel Once the process has taken place, pressure exerted from within the bowel forces the wedge of mucous membrane further along the connective-tissue sheath of the blood-vessels, and eventually a flask-shaped diverticulum is formed When this stage is reached, the circular muscle-fibres between the diverticula steadily contract, so that the pouches become progressively larger, and at the same time the lumen of the bowel becomes narrowed From these considerations it seems impossible to escape the view that diverticula are due to forces arising within the bowel-wall itself

Pathology.—The processes which occur in the diverticula eventually produce inflammatory changes, so that perforation, stricture, and fistulæ result In the great majority of cases, however, diverticulitis runs a chronic, uncomplicated course It is generally acknowledged that pathological changes occur most frequently in the pelvic colon and rectum, probably because of the fæcal stasis which arises at these situations. It is pointed out that, at this level, the nature of the fæces, which are firmer and more compact, tends to prevent the diverticula

tion, later they spread to the other coats of the bowel and to the mesentery, producing perisigmoiditis The chronic thickening of the mesentery results from spread of the inflammatory process, and sometimes may be due to perforation into the mesentery Perforation of a diverticulum may produce a local abscess, or fistula, rarely, however, does it bring about general peritonitis It is not uncommon for a vesico-

present, is probably dependent upon attachment to, or perforation of some other viscus. Diverticulitis with the accompanying pain, pyrexia and leucocytosis, closely resembles appendicitis, but is on the *left* side,

TABLE XVII.—PHYSICAL CHARACTERISTICS OF TUMOURS OF THE COLON

	Carcinoma	Diverticulitis	Bilharziasis	Amœbiasis	Tuberculoma	Actinomycosis
Size and Shape	Fusiform or round	Indefinite and diffuse	Irregular lobulated tumours.	Nodular.	Oval or round.	Indefinite masses
Position (in order of frequency)	Sigmoid, cæcum, transverse colon	Sigmoid, cæcum	Sigmoid, transverse colon.	Sigmoid	Cæcum.	Cæcum mainly.
Mobility	Mobile in early stages Later fixed to surrounding structures	Fixed	Not usually mobile	Mobile.	Fixed.	Fixed
Hardness	Hard and firm	Elastic.	Extremely hard.	Comparatively soft	Hard.	Diffuse.
Tenderness	Usually not tender	Not tender unless in acute stage.	Not tender.	Definitely tender	Not tender	Tender.
Constancy	Preserve their size and shape from day to day.	Inconstant, vary in shape and size from day to day.	Remarkably constant in shape and position.	Conrtant in shape and position.	Constant in shape and position.	Inconstant, usually accompanied by sinuses.



Photo Dr Bertram Shires

Barium enema, showing stenosis and ulceration of the lower sigmoid and rectum in a case of diverticulitis producing dysenteric symptoms. The cæcum had been removed eleven years previously for this condition.



Photo Dr G Mather Cordiner

Barium enema of extreme case of diverticulosis of the transverse colon. (*Dr N H Fairley's case*)

DIVERTICULITIS AND DIVERTICULOSIS

PLATE XX



Photo Dr F G Wood

RADIOGRAPH OF A TUMBLER IN THE RECTUM (*see p* 528)

(*Mr H E Griffiths' case*)

PLATE XXI

and it may be acute, subacute, or chronic Constipation is usually a constant accompaniment, especially when tumefaction has taken place, and an actual lump can be felt On the other hand, diarrhœa alc

acc

ha

consisted for a time almost entirely of blood-stained mucus The explanation of these cases seems to be that the diverticular mass is

has taken place in conjunction with diverticulitis, then the resemblance to the dysenteric syndrome may be very close

The most striking case in the author's series was the following —

was found to be diverticulitis Repeated microscopic examination of the

colostomy had to be performed on account of intrapelvic suppuration

It was definitely proved that the whole illness was due to complications of diverticulitis, no evidence of neoplasm was forthcoming

Symptoms referable to the bladder often occur and usually betoken serious complications, diverticulitis being the most frequent cause of vesico-colic fistula

Complications.—

frequent, and J A B

often in diverticulitis

intraperitoneal absce

There appears to be

to give rise to carcinoma

Amœbic infection may be grafted upon diverticulitis, and may then be responsible for some of the symptoms This complication has been



RADIOGRAPH OF A TUMBLER IN THE RECTUM (see p 528)

(Mr H E Griffiths' case)

PLATE XXI

ceptum; the *neck* is the junction of the entering layer with the mass, and the part which advances is known as the *apex*. The mass which constitutes the main intussusception gathers solidity as it advances. Naturally, with increasing pressure, the blood supply of the inner layers of the intussusception tends to be cut off. Gangrene may, therefore, ensue.

The following varieties of intussusception are recognized —

Ileo ileal	about 8 per cent
Ileo colic (ileo ileal which has passed through the ileo-cæcal valve)	36 ,, ,,
Ileo cæcal (with the ileo cæcal valve at the apex)	46 ,, ,,
Cæcal (invagination of the caput cæci)	2 ,, ,,
Colo-colic (colon invaginated into colon)	8 ,, ,,

In a few cases, intussusception in children arises from irritation caused by a polyp, a submucous lipoma, or a Meckel's diverticulum. In bacillary dysentery in children under ten years of age other infections of the intestinal tract, especially with *Ascaris lumbricoides*, may be a predisposing cause.

Symptoms —Intussusception accounts for the majority of cases of acute intestinal obstruction in children in the first two years of life. It usually occurs in a well-nourished healthy child. He is suddenly

diarrhœa sets in, with blood and mucus in the stools. Indeed, the dis-

noted blood and mucus in 89 per cent of the 400 cases they pass in review. The bleeding arises from venous congestion and, in addition, there is considerable sloughing of tissues

noted twice in the author's series. There is no evidence, however, that a previous dysenteric infection in any way predisposes to diverticulosis. This point has been investigated in seventeen consecutive cases under the author's care.

Diagnosis.—The diagnosis of diverticulosis and diverticulitis is made chiefly by X-ray examination. In the early stages the X-ray appearances are those of extreme irritability of the colon. The signs are those of spasm and excessive motility, all degrees being visible. At first there is marked and irregular haustration. The actual diverticula are visualized as "pinhead elevations" and are usually seen in the sigmoid colon. Then there is the "saw-edge" appearance, and finally well-marked diverticula with wide mouths can be visualized after partial evacuation of the barium enema. (Plate XX.) Diverticula containing fæcoliths give the appearance of grape-like projections from a broad stem, represented by the contracted and spastic bowel.

Proctoscopic and sigmoidoscopic examinations are usually of little value, except when the lesion is extremely low. Sacculation of the mucosa is generally present.

Treatment.—The treatment of diverticulitis is mainly medical; only when complications are present should surgical interference be ... treatment should consist of rest in bed, a

In a patient who presents symptoms of diverticulitis such a regime must be continued indefinitely.

INTUSSUSCEPTION

... it is nevertheless one of
... dysentery, on account
... with one or other of the
...ysentery. So frequently

... intussusception. On the other hand, intussusception may closely simulate bacillary dysentery.

Skin tabs surrounding the anal margin are the result of fibrosis following some acute inflammation, resulting in thrombosis. These tabs are composed of skin, with a central stroma of connective tissue

Internal hæmorrhoids are varicose tributaries of the middle and superior hæmorrhoidal veins, and are situated in the lower 3 or 4 cm of the rectum. Tumours projecting through the anus are classified as internal hæmorrhoids if they are covered by mucous membrane only

Complications of internal hæmorrhoids are chiefly bleeding and prolapse Sometimes excoriation of thrombosed piles occurs, with sloughing and ulceration The amount of bleeding varies consider-

the patient's life, or continuous bleeding from internal piles may bring about a severe macrocytic anæmia, resembling Addisonian

of the many forms of dysentery

In making a diagnosis of internal piles a proctoscope should always be employed, as they may easily be missed by rectal palpation alone

FOREIGN BODIES IN THE RECTUM

Foreign bodies accidentally swallowed may lacerate the mucosa of the rectum on being passed, and may in this manner give rise to dysenteric symptoms Small bones of fish or chicken, for instance, are often passed by children, while adults frequently swallow pins and

cases have been recorded in which the foreign bodies have been recovered several months or even several years after being swallowed

Foreign bodies introduced into the rectum —Remarkable lists have been compiled of foreign bodies which have been introduced through the anus into the rectum either designedly or by accident

Such bodies have been introduced with the intention of relieving

Insane persons

known to conceal

Mummery cites

a box of carpenter's

bacillary dysentery (*see* p. 81). Only in chronic intussusception, which usually occurs in adults, is radioscopy by means of a barium enema of any direct diagnostic value. The need for differential diagnosis from Henoch's purpura may occasionally arise.

When other data are typical, the diagnosis should be made even in the absence of an abdominal mass, as delay in operation is fatal.

Treatment.—The treatment of intussusception is surgical.

HÆMORRHOIDS

Hæmorrhoids are usually sufficiently distinctive to be recognized at sight, but there are many other conditions with which they may be associated. The almost constant association of piles with increased intra-abdominal tension, as in cirrhosis of the liver, is well known, and they also result from portal thrombosis due to porto-systemic anastomosis. They are, therefore, a frequent accompaniment of the dysenteric diseases; the association of external and internal piles with chronic amœbic dysentery has already been referred to (p. 167). The following are some of the conditions from which hæmorrhoids must be differentiated.

Condition	*Means of Differentiation*
Per anal condylomata	Positive Wassermann reaction, history.
Low rectal polypi	Digital examination
Bilharzial adeno-papillomata	Presence of bilharzia eggs in fæces
Amœbic ulceration	*E. histolytica*, free forms, or cysts in fæces.
Carcinoma of rectum	Digital examination.
Polyposis	Digital examination
Granular rectitis	Proctoscopic examination.
Rectal prolapse	Appearance of prolapse
Rectal stricture	Digital examination.
Anal tuberculosis	Appearance of ulceration and bacteriological examination of discharge

Their usually distinctive and characteristic appearance may be modified by thrombosis, ulceration, œdema, necrosis, and even gangrene.

External hæmorrhoids are due to distortion of the veins beneath the skin surrounding the anal margin. Recurrent inflammation leads to

Appendices

tools into his rectum. Death in great agony took place seven days later, and at post-mortem the box, measuring six inches by five and weighing twenty-two ounces, was found, containing several tools, including a screwdriver and a saw. Portions of glass or actual tumblers have been introduced. E. A. Diggins recounts the recovery of a glass from the rectum of a marine engineer in San Francisco Being conscious of certain symptoms in the rectum he touched something which felt like the rim of a tumbler and broke off part of the edge of the glass leaving a serrated margin The tumbler was eventually removed in safety by filling it with plaster of Paris.

The following case, in the Albert Dock Hospital in London, was treated by my colleague, H. E. Griffiths, F.R.C.S., who has kindly permitted me to quote it.

The patient was a boatswain of the

(Plate XXI) was taken as soon as he had been admitted into hospital, and it was found that the tumbler was situated completely above the sphincters, which had contracted below it. Great swelling of the mucous membrane had taken place, so that it entered the lumen of the tumbler and the rim fitted into a sort of groove between the wall of the rectum and the invaginated mucous membrane It was thus impossible to approach the actual rim of the tumbler. The abdomen was opened, and while an assistant exerted pressure upwards

closed A few weeks later he returned to his ship and has been at sea ever since

APPENDIX I

THE INTESTINAL PROTOZOA

ENTAMŒBA HISTOLYTICA (Schaudinn, 1903)

Synonyms.—"*Amœba dysenteriæ*" (Councilman and Lafleur, 1891) *Entamœba coli* var tetragena (Viereck, 1907) *Entamœba hartmanni* (Prowazek, 1912) *Entamœba dysenteriæ* (Councilman and Lafleur) *Entamœba dispar* (Brumpt, 1925)

Historical.—(*See* p 22) It is generally agreed that the amœba first seen by Losch in 1875 and named by him "Amœba coli" corresponds to the

[illegible]

development of amœbæ in the cysts and their emergence in moist preparations of fæces outside the human body A W Sellards and M Theiler (1924)

[illegible]

[illegible] and that the *minuta* really constitutes the precystic form

34

It may be stated categorically that *any amœba found in a dysenteric stool and containing red blood corpuscles is E. histolytica*. Sometimes, when the stools

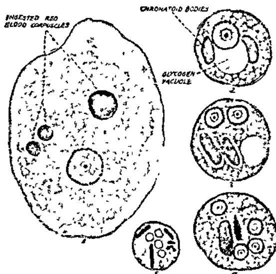


Fig. 93.—*Entamœba histolytica* (× 2,500). (*After Dobell.*)

1, Active amœboid form with ingested red blood-corpuscles. 2, Uninucleate cysts. 3, Binucleate cyst. 4, Quadrinucleate cyst. 5, Quadrinucleate cyst, small race 6μ in diameter.

do not contain blood and are diarrhœic, the amœbæ do not contain red blood-cells, but maintain the morphology characteristic of this species. However, even when the majority do not contain blood-cells, careful search will usually disclose one or two that do.

Other amœbæ, for instance E. col [illegible]

Yorke and Adams (1927) have shown, from clinical and experimental data, that the quadrinucleate cysts take six to eight hours to develop from the precystic stage in the gut, and that the whole cycle, from the precystic stage through the mature cyst to the excysted quadrinucleate amœbulæ, can be passed through in twelve hours. The author has noted that in the human body formation of cysts from precystic stages takes about sixteen hours, as observed in patients in the course of practice. In a recent instance the patient passed in the laboratory at 4 p.m. a stool containing numerous typical active precystic *E. histolytica*, and at 8 a.m. on the following morning a fresh stool showed only typical four nuclear cysts.

Propagation.—The cysts of *E. histolytica* leave the body in various stages of development, seldom are more than 50–60 per cent. mature when first passed in the fæces, but it has been observed by W. Yorke and A. R. D. Adams (1926) that immature cysts can complete their development outside the human body. It has been found, also, that these cysts, when kept moist and cool and when placed in clear water, may live for a number of weeks, but that they are destroyed rapidly by desiccation or by exposure to high temperatures.

E. histolytica cysts begin to die fairly rapidly in fæces kept at laboratory temperature (16–20° C.) for three or four days, and are usually all dead in ten days; the same results are obtained when they are kept at 0° C. in the ice-chest. Washed suspensions live longer, especially at freezing point, but even under those conditions, the majority do not live more than three weeks. The cysts can survive a temperature of 45° C. for thirty minutes, but are killed within five minutes at 50° C. (The author sent specimens to Drbohlav in Prague, and from these a kitten was infected successfully ten days later.)

Resistance to chemicals.—Yorke and Adams have found that cysts are remarkably resistant to emetine and quinoxyl and relatively so to hydrochloric acid and chlorine. By employing the culture viability test, they found that a 1 : 2,500 solution of bichloride of mercury killed cysts in thirty minutes; a 1 per-cent. solution of carbolic or lysol was equally effective. Formalin, on the other hand, is a comparatively poor agent for their destruction. Permanganate of potash is even less effective. Extended observations by many workers, on the action of substances in water, show that the treatment of water with chlorine cannot be relied upon as a means of exterminating the cysts of *E. histolytica*, because it takes practically a hundred times as much chlorine to kill them as is used in water sterilization, and when so treated it is not potable.

The usually-accepted method of determining the vitality of cysts of

The *nucleus* is so delicate that it is practically invisible in fresh and active forms, but when the organism is fixed and stained it presents a characteristic structure. The nuclear membrane is encrusted with uniform fine granules of chromatin and there is a small dot like central karyosome. Between this karyosome and the nuclear membrane there is a clear area which is devoid of chromatic granules and which is marked by a *linin* network with a radial arrangement. From details such as these the nucleus can be distinguished from that of *Entamœba coli*.

Multiplication takes place by binary fission, and normally occurs in the [illegible]

relatively larger nuclei, they then round up and become inactive—in the *precystic stage*. It was formerly thought that the occurrence of this stage was due to unfavourable external conditions, but it is now, apparently, regarded as a naturally recurring phenomenon in the life cycle, irrespective of environment.

Cysts.—Cyst formation then takes place, the sole purpose of which, according to W. Yorke and A. R. D. Adams (1926), is the transmission of the parasite from one host to another.

Before encystment all the food contained in the amœba is thrown out. A thin cyst-wall is formed, thinner and more transparent than that of *Entamœba coli*, and the nucleus remains about one-third of the diameter of the newly-formed cyst. They are then known as *pre cystic* forms.

In the interior of such cyst individuals, there are laid down in the cytoplasm one or two massive and deeply staining structures known as *chromatoid bodies*; in *E. histolytica* they are dumbbell like structures with rounded ends, thus [illegible]

possesses well-marked glycogen vacuoles.

In size, the cysts vary from 5μ to 20μ in diameter, thus corresponding to the various small races of *E. histolytica* which have been described. In fresh preparation they are greenish and are especially refractile, so that they may easily be picked out, with a low power objective slightly out of focus, as minute diamond like structures. On staining with Weigert's iodine, the [illegible]

thickening of the layer of chromosome granules towards one pole of the nucleus, and that this eccentric thickening, since it does not occur in the nuclei of *E. coli* cysts, may be a useful diagnostic guide.

from amœbic dysentery, in a few instances these animals have developed abscesses of the liver Cyst formation can even be produced and accurately controlled in culture tubes (Dobell)

C. Dobell, in a Report of the Medical Research Council for 1931–32, states that the presence of certain bacteria is favourable to the growth of *E histolytica*, while that of other organisms is harmful, so that special bacteria seem to have a special relation to events in the life-cycle The entamœba is unable to form cysts in culture, unless this particular bacterial species is present, and they are unable to "hatch" in sterile media or in the presence of *dead* bacteria These circumstances may shed light on the conditions which cause *E histolytica*, when present in the lumen of the healthy human intestine, to assume a pathogenic rôle in the tropics

Susceptibility of animals to E histolytica infection—F Lösch (1875) first

the surface of the large intestine is infected with amœbæ, commencing at the lower part of the large intestine, where changes in the mucosa are most marked A W Sellards and L Leiva (1923) have shown that it is at this point that natural stasis occurs By ligaturing the large intestine of cats at various levels and inoculating material containing amœbæ directly into the cæcum, they demonstrated that the infection commences and is most marked just above the ligature If the animal survives long enough definite ulcers occur, as in human beings, but usually death takes place from general necrosis of the mucosa As these observers have shown, bacterial invasion of the blood plays a decisive part Heavily infected cats pass *per anum* a whitish fluid containing broken down cells and enormous numbers of amœbæ, in the less acute stages the stools resemble those of amœbic dysentery in man Recovery rarely takes place in cats, but when it occurs the infection entirely dies out, no carrier condition being produced, as in man Secondary infection of the liver may take place, leading to liver abscess

Guinea-pig—Guinea pigs have been infected by Baetger and Sellards (1914) and later by other workers, infection being brought about by injection

found in monkeys (*Macacus sinicus* and *M rhesus*) is identical with

Amœbic dysentery and amœbic liver abscess may occur in animals in captivity as a natural infection. A Eichhorn and B Gallagher (1916) record a case of dysentery complicated by liver abscess in an orang utang in Manila In an outbreak in America, spider monkeys (*Ateles ater*) were infected; out

cats It appears that the viability of cysts is dependent, not merely on the amount of available moisture, but also on the prevailing bacterial flora Kuenen and Swellengrebel (1913) in carrying out a series of experiments, showed, for instance, that at a temperature of 27–30° C. cysts kept in water containing bacteria were no longer viable after nine days, but a proportion remained so for twenty-nine days at lower temperatures, when the bacterial flora was not excessive. W. C. Boeck (1921) showed, further, that cysts stored in distilled water and subjected to thorough washing could survive for 153 or even 211 days.

It is only in the cystic stage that amœbæ can survive outside the body, and it is only by cysts that infection may be spread. Free forms appear to be unable to pass through the human stomach, although C. Dobell and P P. Laidlaw (1926) found that motile amœbæ could withstand 0 2 per cent. hydrochloric acid for thirty minutes.

The *amœbulæ* escape from the cysts (Yorke and Adams) in a suitable medium at body temperature The quadrinucleated encysted amœba produces a new generation of trophic forms by a complicated series of nuclear and cytoplasmic divisions The final result is the production of eight uninucleate amœbulæ by each quadrinucleate amœba hatching from the cyst. These amœbulæ are young trophic amœbæ and not gametes or conjugants. No sexual phenomena of any sort have been observed during the metacyclic stages, and the life history of *E histolytica*, as visible *in vitro*, is wholly asexual (C. Dobell, 1928)

Culture.—The knowledge that active free *E histolytica* can successfully be cultivated outside the human body we owe to the work of Boeck and

In cultures of the cysts, the uninucleated and binucleated forms rapidly become quadrinucleated, and the nuclei tend to group together towards the centre. The chromatoid bodies form and finally disappear, and so does the glycogen

The process of excystation is preceded by the withdrawal of the proto-

of the nine showing symptoms, only one recovered, and liver abscesses containing amœbæ were found at autopsy in two

R. Hegner, C. M. Johnson, and R. M. Stabler (1932) have produced amœbic infections in American monkeys belonging to seven species, including the brown howler monkey, the red spider monkey, and the marmoset. They found in these animals tissue-dwelling amœbæ in the tissues of the intestinal wall, and *lumen-amœbæ*, living in the lumen of the intestine, but not invading the bowel-wall. Injuries of the intestinal wall due to amœbæ were observed in all the twelve infected monkeys examined post-mortem. It was found that

depth, and their histological structure are comparable with those found in man. The signs of amœbic enteritis in the dog include acute fulminating dysentery, chronic enteritis, and convalescent carrier conditions, as well as temporary infections followed by apparent spontaneous recovery. Amœbic hepatitis has been observed in these animals and H. F. Harris (1901) recorded an amœbic liver abscess.

Rat.—J. F. Kessel (1923) claimed that he infected rats with *E. histolytica* and that natural infection of these animals with the parasite may occur. The infection artificially produced is chronic and persists for months. The amœbæ from experimental rats, as well as the naturally-occurring rat strain (*E. histolytica murina*), can give rise to typical symptoms when injected into a kitten. S. F. Chiang (1925) succeeded in repeating this work and regards the rat as possible reservoir of the infection for man.

ENTAMŒBA COLI (Grassi, 1879; Casagrandi and Barbagallo, 1895)

Synonyms.—*Amœba coli* (Grassi, 1897). *Entamœba williamsi* (Prowazek, 1911). *Councilmania lafleuri* (Kofoid and Swezy, 1921).

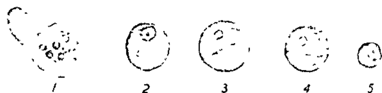
Entamœba coli is of interest to the practical physician chiefly because of its close resemblance to *E. histolytica*. It is necessary that this protozoon should be recognized in all its stages in order that it may be differentiated from the pathogenic amœba. (Fig. 94.)

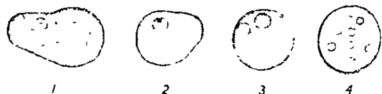
E. coli lives in the lumen of the human large intestine; it has never been found to invade the tissues. It feeds mostly on the bacteria in the bowel, on starch granules, and on yeasts, and it may even, on occasion, ingest other protozoa such as cysts of *E. histolytica*, *Giardia*, and *Isospora hominis*. It does not, like *E. histolytica*, ingest red blood-corpuscles, although K. M. Lynch (1924) has shown that it can be induced to do so on artificial culture. The free forms vary in size from 10 μ to 40 μ in diameter; extremes in size are by no means so common as in *E. histolytica*, the majority measuring from 15 μ to 30 μ.

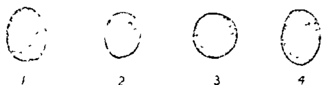
There are two protoplasmic layers, as in *E. histolytica*, but the ectoplasm is not so evident and can only be made out when a pseudopod is extended. In its movement *E. coli* is slow; it appears to protrude pseudopodia in all directions when ingesting food material, but it does not itself progress, remaining fixed to one spot.

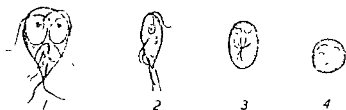
The *endoplasm* has a close, coarse, granular appearance, and is usually vacuolated; it may be very difficult, or almost impossible, to distinguish between it and degenerate trophozoites of *E. histolytica*.

The *nucleus* is spherical and vesiculated and possesses an achromatinic nuclear membrane, usually thicker and more prominent than that of *E.*











P H Manson Bahr del

ESTINAL PROTOZOA (unstained)

PLATE XXII

PLATES XXII AND XXIII

INTESTINAL PROTOZOA

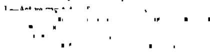
Row A. *Entamœba histolytica* (Unstained)

1.—Active vegetative form with ingested red blood-corpuscles granular endoplasm and clear ectoplasm
2.—Precystic form Note large nucleus with central karyosome
3.—Immature cyst with two nuclei and contained chromatoid rods
4.—Mature cyst with four nuclei, vacuole and chromatoid rods
5.—Uninucleated cyst of the minuta stage

Row A_1 *Entamœba histolytica* (Stained Weigert's Iodine)

1.—Precystic form Note diffuse iodine-staining substance
2.—Immature cyst with two nuclei and chromidial rods
3.—Mature cyst with four nuclei, iodine vacuoles and chromidial rods
4.—Quadrinucleated cyst of the minuta stage

Row B *Entamœba coli* (Unstained)



Row B_1. *Entamœba coli* (Stained Weigert's Iodine)

1.—Active vegetative form with vacuoles and ingested food material
2.—Precystic form
3.—Immature cyst with two nuclei and vacuole
4.—Mature cyst with eight nuclei

Row C *Endolimax nana.* (Unstained)

1.—Active vegetative form with one nucleus and many small vacuoles
2.—Mature cyst with four nuclei.

Iodamœba butschlii. (Unstained)

3.—Active vegetative form with one nucleus and large vacuole
4.—Mature cyst with one nucleus and large vacuole

(*Continued overleaf*)

PLATES XXII AND XXIII

INTESTINAL PROTOZOA (*Continued*)

Row C_1. *Endolimax nana.* (Stained Weigert's Iodine.)

1.—Active vegetative form with one nucleus and protoplasmic granules

2.—Mature cyst with four characteristic nuclei and iodine-staining substance

Iodamœba butschlii. (Stained Weigert's Iodine.)

3.—Active vegetative form with one nucleus and iodine-staining vacuole

4.—Mature cyst with one nucleus and iodine-staining vacuole

Row D. *Giardia intestinalis* (Unstained.)

1.—Active form with sucking disc.

2.—Active form (side view).

3.—Cyst with two dividing nuclei

4.—Four nucleated cyst (end-on view)

Row D_1. *Giardia intestinalis.* (Stained Weigert's Iodine.)

1.—Active form with sucking disc

2.—Active form (side view).

3.—Cyst with two dividing nuclei

4.—Four nucleated cyst (end-on view)

Row E. *Trichomonas hominis.* (Unstained.)

1.—Active form with undulating membrane and supporting rod

Chilomastix mesnili. (Unstained.)

2.—Active form with peristome and contained flagellum

3.—Pear-shaped cyst of above

4, 5, 6.—Various forms of *Blastocystis hominis*

Row E_1. *Trichomonas hominis* (Stained Weigert's Iodine.)

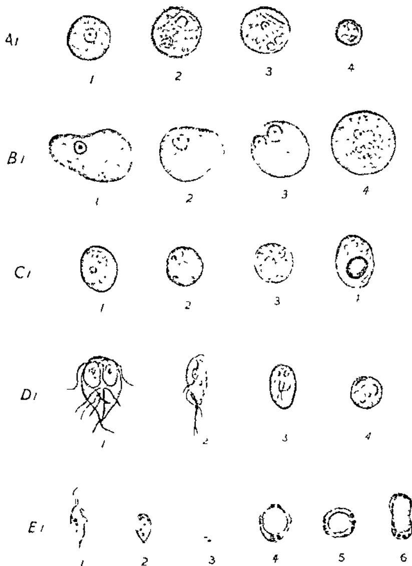
1.—Active form with undulating membrane and ingested red blood corpuscles the latter is an occasional occurrence

Chilomastix mesnili (Stained Weigert's Iodine.)

2.—Degenerated form as it commonly appears when acted upon by iodine

3.—Pear-shaped cyst of above with nucleus and peristomes

4, 5, 6.—Various forms of *Blastocystis hominis.*



HUMAN INTESTINAL PROTOZOA
(Stained with Weigert's iodine)

PLATE XXIII

histolytica The nucleus is filled with a fluid through which a *linin* reticulum is spread The *chromatin* of the nuclear membrane occurs in large masses and is more irregular than that of the *E. histolytica* nucleus The *karyosome* is placed excentrically within the nucleus, and in stained preparations is surrounded by a clear space termed a *halo*

Multiplication in *E coli* is by binary fission and this process appears to be initiated in the karyosome The nucleus divides by a modified mitotic process into two daughter nuclei, each of which possesses the same characters as the parent nucleus

Propagation of *E coli* is by means of resistant cysts Before encystment

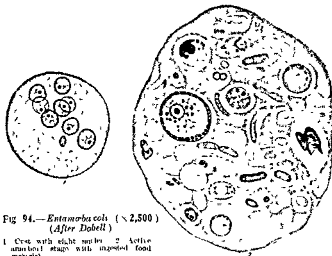


Fig 94.—*Entamœba coli* (×2,500) (*After Dobell*)

1 Cyst with eight nuclei 2 Active amœboid stage with ingested food material

the vegetative amœbæ become smaller and void any foodstuffs they may have ingested Th [illegible]
round [illegible]
than tha [illegible]
those of [illegible]
but usua [illegible]
typo of cyst most commonly found in the stools is one which contains eight nuclet

The newly formed cyst contains a considerable amount of glycogen, acicular shaped chromatoid bodies, and a nucleus which has the characters of the free form This nucleus soon divides into two, then into four, and finally into eight, very occasionally cysts are found which contain as many as sixteen The contained glycogen can be demonstrated when stained

from the cysts. Occasionally vacuoles appear round the periphery of the cyst while the cytoplasm with contained nuclei occupies the centre. (Plates XXII, XXIII, B, 1–4.)

E. coli can be cultivated, but with considerable difficulty, on the medium of Boeck and Drbohlav (1925). These workers, and also J. G. Thomson and A. Robertson, have managed to keep strains alive for a considerable period.

ENDOLIMAX NANA (Wenyon and O'Connor, 1917; Brug, 1918)

Synonyms.—*Entamœba nana* (Wenyon and O'Connor, 1917). *Endolimax intestinalis* (Kuenen and Swellengrebel, 1917).

This is one of the most common protozoa of the human intestinal canal, and is certainly non pathogenic. It occurs in quite a large proportion of the normal human population, a percentage of 2·4 being found by J. R. Matthews

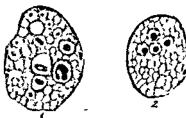


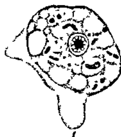
Fig. 95.—*Endolimax nana* (× 2,500.)
(*After Dobell.*)
1, Active amœboid form; 2, Quadrinucleate mature cyst.

(Plates XXII, XXIII, C, 1–2.)

observed. When mature, the *cyst* contains four nuclei which are usually grouped together at one pole of the cyst. The nuclear characters are similar to those of the free forms, but they are smaller. Cysts vary from 8 μ to 10 μ in length by about half that in breadth and are usually very numerous.

Endolimax nana has been cultured, with difficulty, on Boeck and Drbohlav egg medium by J G Thomson and A Robertson (1925)

IODAMŒBA BUTSCHLII (Prowazek, 1912, Dobell, 1919)



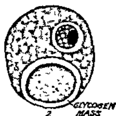


Fig. 96 —*Iodamœba butschlii* (× 2,500) (*After Dobell*)
1, Active amœboid form with ingested micro-organisms, 2, Mature cyst iodine cyst, containing large glycogen mass

A remarkable feature of this infection in man is the immense number of cysts which are passed without the ascertainable presence of free forms (Plates XXII, XXIII, C, 3–4)

disappear

Most cysts contain only one *nucleus*, though cysts with two nuclei are not uncommon in some infections In this amœba there is apparently no definite

precystic stage, or at any rate a reduction in the size of the organism does not occur. All foodstuffs are removed from the cytoplasm, which now becomes clear, transparent, and finely granular in appearance. The cyst-wall is secreted and soon glycogen appears to be produced.

DIENTAMŒBA FRAGILIS (Jepps and Dobell, 1918)

Synonym.—*Histomonas fragilis*

This amœba is seldom found in fæces and is by far the least frequent of all the human intestinal amœbæ. The reason advanced for its apparent scarcity is that it is highly susceptible to small variations in temperature and, directly the fæces become chilled on passing out from the body, becomes *spherical and motionless*, thus escaping detection.

D. fragilis is comparatively small in size, from 3 μ to 12 μ in diameter. The cytoplasm is sharply differentiated into ectoplasm and granular endoplasm. (Fig. 97.) The pseudopodia are active and tend to be conical in outline, are in fact leaf like (Dobell), and they may give rise to secondary smaller pseudopodia. The endoplasm is finely granular, and may be vacuolated and contain bacteria and ingested food material. The majority



Fig. 97.—*Dientamœba fragilis*, uninucleate and binucleate forms (× 2,500.) (*After Dobell.*)

of the free forms are binucleate and have the nuclei situated near to one another. It is thought probable that these binucleate amœbæ are the mature individuals which on division give rise to uninucleate forms. The *nucleus* is a fine structure and has an achromatinic nuclear membrane. The nuclear chromatin is arranged in a ring of granules, four, five, or six in number, midway between the central point of the nucleus and the nuclear membrane. So far no workers have described encysted forms.

From his intimate studies of *E. fragilis* in monkeys, C. Dobell (1940) has now modified his views on its morphology. As seen in culture, the forms possess two nuclei connected by a thread (*centrodesmose*) resembling the flagellate *Histomonas meleagridis*, the cause of "blackhead" in turkeys. This normally lives as a flagellate in the cæcum, but can invade the liver,

GIARDIA INTESTINALIS (Lambl, 1858, Alexeieff, 1914)

Synonyms.—*Lamblia intestinalis* (Lambl, Blanchard, 1855) *Giardia* ... (Stiles, 1915)

by having a body
...al surface is convex,
a posterior tapering

tail which is a flexible structure that can be turned up over the convex dorsal surface. The remainder of the body is rigid. On the ventral surface there is a sucking disc, almost circular in outline save for a posterior orientation, which is provided with a raised edge. By means of this disc the flagellate is able to rest attached to the surface epithelium of the bowel. It has four pairs of flagella, symmetrically arranged, and two nuclei, one lying on each

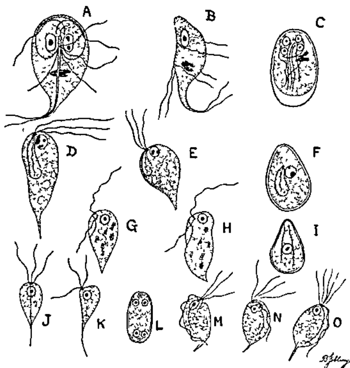


Fig 98.—The flagellates of the human intestine. (× 2,000)
(*After Wenyon, by permission*)

A–C, *Giardia intestinalis*, free and encysted forms. D–F, *Chilomastix mesnili*, free and encysted forms. G–I, *Embadomonas intestinalis*, free and encysted forms. J–L, *Tricercomonas intestinalis*, free and encysted forms. M–O, *Trichomonas hominis*, forms with three, four and five flagella.

side of the middle line of the body. When swimming, the active form sways from side to side, like a flat fish passing through a liquid medium. The internal structure is somewhat complicated (Fig 98, A–C).

Reproduction takes place by binary fission and is usually accomplished within an ovoid which first forms round the anterior end of the body and, expanding backwards, gradually encloses the tail, which is finally retracted

within the cyst-wall In a rece-

the tail may be seen moving wit

cyst so that eventually two sepa

accompanying organs, lie inside;

be mistaken for a four-nucleated

The cysts of *Giardia* persist in the stools for years, the numbers varying considerably from time to time Cases have been observed by the author

O'Connor in 1917 found that it was present in 4 1 to 16 per cent of normal individuals in Egypt, while C. Dobell estimated that 18 to 27 per cent of the artisan population of the British Isles harboured this flagellate. W. C. Boeck and C W Stiles (1923) found it in 48 1 per cent of school children in America.

TRICHOMONAS HOMINIS (Davaine, 1860)

Synonyms.—*Cercomonas hominis* (Davaine, 1860). *Trichomonas intestinalis* (Leuckart, 1879).

T. hominis inhabits the human intestine, where, probably, it is quite harmless It is usually rounded or oval, but it can adopt a great variety of shapes It measures 10 μ to 15 μ in length by 7 μ to 10 μ in breadth. (Plates XXII, XXIII, E, 1)

At the anterior end of the parasite there is a mass which stains deeply and is a congregation of blepharoplasts from which arise flagella, usually four in number. The nucleus, situated at the anterior end, is round and vesicular. There is also a thick strong lateral flagellum which, passing backwards from the blepharoplasts, serves as the outer margin of a wide undulating membrane At the further end of the parasite it becomes free for a short distance. A small aperture near the anterior end represents the mouth, or cytostome Within the body of the parasite, passing from the blepharoplast to the poster-

According to the number of free flagella (three, four or five), three varieties of *Trichomonas* have been described

Multiplication takes place by binary fission, but no cysts of this organism are known Cultivation can easily be effected on Boeck and Drbohlav's Locke egg-medium

CHILOMASTIX MESNILI (Wenyon, Alexeieff, 1910)

Synonym.—*Tetramitus mesnili* (Wenyon, Alexeieff, 1910)



(Plates

which produces characteristic, lemon-shaped cysts, measuring 7 μ to 9 μ in length The mature cyst contains a single nucleus of much the same appearance as that of the trophozoite (Fig 98, D–F)

TRICERCOMONAS INTESTINALIS (Wenyon and O Connor, 1917)

Synonym.—*Enteromonas hominis* (Fonseca, 1915)

This parasite was discovered by Wenyon and O'Connor in 1917 in Alex



from this arises the fourth flagellum which runs to the posterior extremity of the body, ending as a terminal lash When the movement is studied in living organisms the combined result of the flagellar lashings imparts a " hovering " effect

The cysts are small and closely simulate fungus spores. They are usually oval with a distinct cyst-wall, and included within them are certain rounded and highly refractile bodies which stain brown with iodine (Fig. 98, J–L.)

EMBADOMONAS INTESTINALIS (Wenyon and O'Connor, 1917)

Synonym.—*Waskia intestinalis* (Wenyon and O Connor, 1917)

E. intestinalis was originally discovered by C M. Wenyon and F. W.

The nucleus is spherical and vesicular, and possesses a distinct nuclear membrane and a large central karyosome. Two blepharoplasts, from which *the flagella originate, are applied to the nuclear membrane.*

The cysts, which measure 4–9 μ by 2–3 μ, are minute pear-shaped bodies in which it is extremely difficult to detect any internal structure.

BALANTIDIUM COLI (Malmsten, Stein, 1862)

Synonym.—*Paramœcium coli* (Malmsten, 1857)

(Fig 99.) At the anterior extremity, and situated somewhat obliquely, is a depression known as the peristome, which marks the ventral surface of the

zones measuring 6–12 μ.

becomes contracted and hour-glass shaped, the cytostome remains within the anterior wall, and a new mouth-cavity is formed. Multiplication in this manner has been observed to take place in the lumen of the bowel, and in the tissues where the parasite has penetrated the mucous membrane. *Conjugating stages have been observed*, *according* to Brumpt, the two ciliates become attached to one another by their peristomes and enclosed in a

succeeded in infecting rats with balantidia from the chimpanzee, by introducing them directly into the stomach

Cultivation —*Balantidium* has been cultivated outside the body by H P. Barret and N Yarbrough (1921) Employing as a medium a mixture of

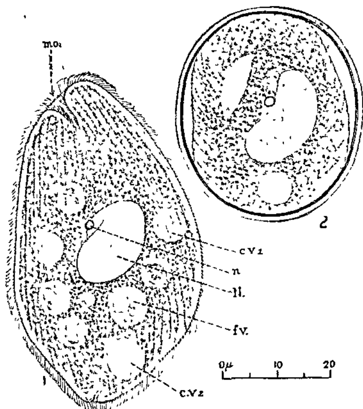


Fig. 99.—*Balantidium coli* (× 1,200.) (*After Dobell, by permission of Medical Research Council, Report No 51*)

1, Living animal, N, meganucleus, n micronucleus c v 1, anterior contractile vacuole, c v 2, posterior contractile vacuole, f v, food vacuole, mo mouth
2, Encysted form, showing nuclei, posterior contractile vacuole, and remains of cilia

inactivated human serum with 0 5 per cent of salt solution in the proportion of 1 in 16, they have been able to cultivate it by subinoculation for fifty-four days.

BLASTOCYSTIS HOMINIS

Blastocystis hominis (Plates XXII, XXIII, F. 2–6), a yeast-like organism which may simulate the encysted stage of an amœba, is very common

in the fæces It multiplies by gemmation and can be recognized on microscopic examination, especially in iodine preparations. It has an irregular oval or bilobed shape. There is a large central vacuole which does not stain with iodine, but there are prominent iodophilic granules in the periphery of the cell which give it a rough resemblance to a double sided signet ring. These organisms vary a good deal in size, from 2-15 μ in diameter. They are found most commonly in dysenteric and sprue stools, but are of no pathological importance

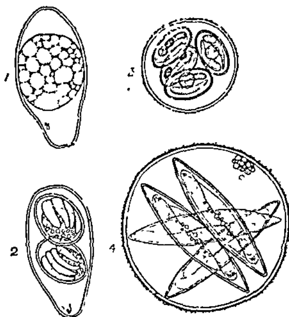


Fig 100—Oocysts of coccidia found in human fæces. (× 1,000)
(*After Dobell*)

1, *Isospora hominis*, undeveloped cyst 2, Fully-developed spores of same, 3, *Eimeria clupearum*, fully-developed oöcyst and spores, 4, *Eimeria sardiniæ*, fully-developed oöcyst and spores

COCCIDIA

The coccidia are intracellular protozoa which inhabit the cells of the intestinal canal and liver of vertebrates. Their life history differs from that of the amœbæ in that they exhibit an alternation of generations in which an asexual cycle, "schizogony," alternates with a sexual cycle, "sporogony" In the latter cycle a single zygote becomes encysted as an oöcyst and eventually produces a number of sporozoites which are included in masses in smaller cysts (sporocysts). The young parasites—or sporozoites—are liberated from a sporocyst in the intestinal tract, they then penetrate epithelial cells, and grow into large schizonts, characterized by a large vesicular nucleus and a karyosome When full-grown the nucleus divides by repeated

fission till a number of daughter nuclei are produced The schizont now divides into as many merozoites as there are nuclei The cell then bursts and the merozoites are set free, enter other cells and develop either into schizonts

considered to be human parasites (Fig 100, 3, 4)

One species only is parasitic in man, though it is not seriously pathogenic

Isospora hominis (Railliet and Lucet, 1901)

Synonym —Isospora belli (Wenyon, 1923) *

As mentioned on p 266, over 150 cases of infection with this organism have now been described in man, most of them hailing from the eastern

* C A. Hoare now considers *I hominis* and *I belli* distinct species, the former being probably a dog parasite accidental in man while the latter is a human species parasitic in the epithelium of the small intestine

APPENDIX II

LABORATORY METHODS

EXAMINATION OF FÆCES

General.—It cannot be over-emphasized that in examination of fæces, whether for the presence of protozoa or of bacteria, the sooner the specimen is examined in the laboratory the more accurate and convincing will be the pathologist's report Indeed, whenever possible, the patient should pass a specimen into a suitable receptacle in the laboratory so that it may be examined while still warm. The patient is provided with a separate vessel for urination, to prevent contamination. The receptacle into which the stool is passed must be clean and free from disinfectants From a bed case the stool should be sent to the laboratory as speedily as possible.

Forwarding samples for examination.—If the patient resides in the town in which the laborator

container, may be

regulations govern

familiar fæces tube-

fixed—must be enclosed in a wooden case and prevented from jolting by packing the top with cotton-wool After suitable wrapping, the parcel is labelled "Pathological Specimen," "Fragile," "With great care" The specimen should be posted late at night or in the early morning and should be examined immediately it reaches the laboratory

In the tropics, if the specimen has to come a long distance, it is sent by native runner Various devices have been utilized for keeping the specimen "fresh," and perhaps the best method for the detection of amœbæ in a

by rendering the medium alkaline, conserves vitality of the organisms for a longer period

Disposal of infected material —For the disposal of fæces tubes after examination of the contents, an enamel bucket provided with a lid is filled three-quarters full with 3 per cent Lysol, this having been found preferable to other "sticky" disinfectants Into this bucket the tubes are dropped after removal of the corks They are left till the bucket is full, and after a few days

tray to drain

Macroscopical Examination of Fæces

Considerable aid in determining the cause of a diarrhœic condition may often be obtained by careful macroscopical examination of fæces, and where possible the whole stool should be inspected The bacillary dysentery stool may often be composed of fluid blood and mucus, while the amœbic usually consists of thick blood and mucus intermingled with fæces It must be realized, however, that the stool of convalescing bacillary dysentery may simulate that of amœbic, or balantidial dysentery, intestinal bilharziasis, or ulcerative colitis

The consistency, colour, smell, and presence or absence of blood or mucus should be noted A fresh bacillary-dysentery stool gives off the odour of spermin or freshly laundered linen, while the amœbic is usually offensive The sprue stool is bulky and may be composed of thick rolls, not unlike farm house butter, or semi-solid material resembling cream. It has a charac-

butcher's meat, and when fluid, resemble pea soup In intestinal tuberculosis the stool usually consists of greenish fæces containing much mucus with little blood, and is very offensive, when associated with intestinal polypi it often bears a resemblance to sputum The stools of rectal carcinoma

mingled with liquid pale fæces, those associated with other flagellate infections are gelatinous, watery, and odoriferous

In Table XX an attempt has been made to tabulate the characteristic stools of different conditions It must, however, be understood that the various

Microscopical Examination of Fæces

If free amœbæ are seen, the following points should be noted: cytoplasm

Disease	Macroscopically	Odour
PANCREATITIS	Bulky, yellowish-white, liquid or semi-solid fæces which "set" in half an hour after passage. No blood or mucus	"Cheesy"
CŒLIAC DISEASE AND IDIOPATHIC STEATORRHŒA	Liquid or semi-solid, bulky, yellowish-white fæces. No blood or mucus	Very offensive
SPRUE	Bulky, fermenting, yellowish-white, *liquid fæces or soft solid fæces like* rolls of farmhouse butter. No blood or mucus	Sour
BACILLARY DYSENTERY	Thin blood and mucus or blood and mucus with greenish liquid fæces	Not offensive, like freshly laundered linen
TYPHOID FEVERS AND PARATYPHOID	Liquid, brown, "pea soup" fæces, sometimes with little thin blood and mucus	Very offensive, like butcher's meat
CHOLERA	*Thin, watery, "rice-water" stools*. No blood or mucus	*Odourless*
AMŒBIC DYSENTERY	Thin blood and mucus, intermingled with normal or liquid fæces. Often only minute quantity of blood and mucus	Offensive
BALANTIDIAL DYSENTERY	Liquid brown fæces intermingled with blood and mucus	Very offensive
GIARDIASIS	Mostly mucus, or liquid fæces with considerable amount of thin mucus. May be light in colour and pasty	Inoffensive
OTHER FLAGELLATE INFECTIONS	Gelatinous, mostly liquid fæces	Offensive
BILHARZIASIS	Semi-solid, chocolate-coloured fæces thick blood and mucus, often in "clumps," may be present or may be intermingled with the fæces	Offensive
MUCOUS COLITIS	"Stringy" mucus intermingled with liquid or semi-solid fæces. No blood, sometimes membrane	Offensive
ULCERATIVE COLITIS	Thick blood and mucus with or without liquid fæces. Sometimes visible pus	Very offensive, like "stale blood"
POLYPOSIS	Dark-coloured blood with small amount of mucus. No visible pus	Offensive
POLYPUS	Whitish, thin mucus with or without fæces. Looks like sputum	Inoffensive
INTESTINAL TUBERCULOSIS	Greenish-brown liquid fæces containing intermingled blood and mucus	Very offensive

Microscopically	Organism
Similar to sprue, but fatty globules present and fatty crystals usually arranged in spheres Undigested food particles "ciliated" Bacteria few	None incriminated
Similar to sprue, but fatty globules may be present Fatty crystals scattered Excess of starches Bacteria plentiful	None incriminated
No pus, mucous or blood-cells Bacteria few Undigested food particles and fatty crystals, the latter arranged in bundles, abundant, fatty globules usually absent Usually numerous *Blastocystis hominis*	Causal organism unknown
Red blood-corpuscles often in "clumps," macrophage, pus, epithelial and shadow cells Bacteria few	Dysentery bacilli by cultural methods
Usually ordinary diarrhoeic picture, but sometimes few red blood- and pus-cells	Typhoid and paratyphoid bacilli by cultural methods
Mucous and pus cells Blood-corpuscles absent Bacteria scanty	Cholera vibrio by cultural methods
Red blood corpuscles, very few pus cells, mucous and epithelial cells Charcot-Leyden crystals, free forms of *E. histolytica*, active, containing R B C s Bacteria numerous	*Entamœba histolytica* Confirmed by appropriate staining methods
Red blood corpuscles, pus, mucous and epithelial cells present Charcot-Leyden crystals absent *Balantidium coli* present Bacteria abundant	*Balantidium coli* Confirmed by appropriate staining methods
Numerous mucous cells, occasionally pus cells R B C s rare Active *Giardia (Lamblia) intestinalis* free if mostly mucus Numerous cysts if mucus scanty Bacteria few	*Giardia (Lamblia) intestinalis* Confirmed by appropriate staining methods
Few mucous cells, no pus-cells *Trichomonas hominis* or *Chilomastix mesnili*, free forms present Bacteria abundant	*Trichomonas hominis*, *Chilomastix mesnili*, etc
Similar to amœbic dysentery Charcot Leyden crystals often present, typical ova of *B mansoni* or *B japonica* present, but usually scanty, rarely, *B hæmatobia*	*Bilharzia mansoni*, *B hæmatobia*, or *B japonica*
Mucous and epithelial cells abundant arranged in "strings" No red blood-corpuscles Undigested food remains abundant Bacteria numerous	No definite organism responsible
Similar to amœbic dysentery, but large numbers of pus and macrophage cells Charcot-Leyden crystals often present Bacteria scanty	No definite organism responsible
Large numbers of red blood corpuscles in clumps Columnar epithelial cells and few pus-cells Bacteria scanty	None incriminated
Mostly mucous cells. Few pus-cells Bacteria scanty	None incriminated
Red blood-cells, pus, mucous and epithelial cells present Bacteria abundant	Tubercle bacillus confirmed by appropriate staining

TABLE XIX.—BIOLOGICAL REACTIONS OF PATHOGENIC AND ALLIED ORGANISMS RECOVERED FROM THE FÆCES

	Mannite		Glucose		Maltose		Lactose		Saccharose		Dulcite		Litmus or Phenol Red Milk			Indole	Motility
	A	G	A	G	A	G	A	G	A	G	A	G	A	Alk	Clot		
Bact. shigæ	0	0	+	0	0	0	0	0	0	0	0	0	+	0	0	0	0
Bact. flexneri	+	0	+	0	+	0	0	0	0	0	0	0	+	+	0	+	0
Schmitz's bacillus	0	0	+	0	0	0	0	0	0	0	0	0	+ sl	0	0	+	0
Sonne's bacillus	+	0	+	0	0	0	+	0	+ or 0	0	0	0	+	0	+	0	0
Bact. dispar	+	0	+	0	0	0	+	0	0	0	±	0	+	0	+	±	0
Bact. morgani	0	0	+	+ sl	0	0	0	0	0	0	0	0	0	+	0	+	+
Bact. typhosum	+	0	+	0	+	0	0	0	0	0	0	0	+	0	0	0	+
Bact. paratyphosum A	+	+	+	+	+	+	0	0	0	0	+	+	+	0	0	0	+
* *Bact. paratyphosum B.*	+	+	+	+	+	+	0	0	0	0	+	+	+	+	0	0	+
* *Bact. enteritidis*	+	+	+	+	+	+	0	0	0	0	+	+	+ sl	+	0	0	+
Bact. coli	+	+	+	+	+	+	+	+	0	0	+	+	+	0	+	+	+
Bact. fæcalis alkaligenes	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0	+
Bact. acidi lactici (Hüppe)	+	+	+	+	+	+	+	+	0	0	0	0	+	0	+	+	0

A = acid, G = gas, Alk = alkaline, Sl = slight

* To differentiate *Bact. enteritidis* and other organisms of the food-poisoning group from *Bact. paratyphosum B* serological tests must be applied

clear or granular, movement sluggish or active, position of the karyosome, presence or absence of included red blood corpuscles It is unusual to find free amœbæ, other than *E histolytica* or *E coli*, in a blood and mucus stool, and to find the latter in inflammatory exudate is such a rare event that, if the morphological differences between these two types are clearly understood, (*see* p 533), mistakes should not occur Unfortunately, *Entamœba histolytica* [illegible]

ous amœbæ. The explanation may lie in the fact that amœbæ are often discharged from the bowel into the fæcal contents in "pockets," and by chance one of these "pockets" was inoculated into the culture medium and another selected by the student If such a "pocket" is fortunately picked up, the microscopic picture is remarkable—dozens of typical amœbæ may be seen in the field It follows, therefore, that in the examination of a stool from a suspected amœbic dysentery case, one negative slide is not sufficient, and several portions from various parts of the stool should be searched If the stool remains negative on one microscopical examination, further specimens should be searched It is a well established fact that amœbæ may be entirely absent on one day, and on the following be extraordinarily abundant This applies equally to cysts

If the stool consists of liquid fæces, a drop of normal saline or 1 per cent watery eosin is placed at one end of a slide and a drop of Weigert's iodine at the other A portion of the fæces is first rubbed into the saline or eosin-solution drop with the aid of a match-stick, and then a portion is emulsified in iodine, and the resultant mixtures, which should not be too thick, are covered with cover glasses The saline or eosin portion of the slide is examined under the ⅙ in -objective for amœbæ flagellates, or cysts After a little [illegible]

an hour or longer until rapid movement has ceased, when the structure becomes more easily discernible

In the examination of a suspected amœbic dysentery stool, care should be taken not to mistake the macrophage cells found in bacillary dysentery and in ulcerative colitis for *Entamœba histolytica* (Fig 101) It is advisable for the beginner never to make a diagnosis of amœbic dysentery unless typical *E histolytica* individuals are seen, showing the characteristic amœboid movement and containing enclosed red blood-cells It must be borne in mind that often only a few of the amœbæ contain ingested red blood-cells Similarly not every *E histolytica* cyst shows the characteristic four nuclei and chromidia Where any doubt exists, staining should be resorted to, for free amœbæ, the rapid phosphotungstic acid hæmatoxylin is recommended, and for cysts the iron hæmatoxylin method (*see* p. 575)

Concentration methods for E histolytica cysts —C F Craig ("Amebiasis and Amebic Dysentery") recommends the emulsification of a portion of fæces

about the size of a pea in 10 c c. of normal saline in a test-tube. This mixture is strained through a double layer of cheese-cloth and is then transferred to a centrifuge tube, which is filled to the top with saline and is centrifugalized at a moderate speed for 3–4 minutes. The sediment is then examined for cysts directly or with the addition of Weigert's iodine.

Yorke and Adams emulsify a walnut-sized portion of the suspected stool in tapwater. The mixture is made up to 500 c c., placed in a tall glass cylinder, and stood aside for half an hour. It will then be found that a scum has formed at the top of the fluid, and a considerable amount of sediment has fallen to the

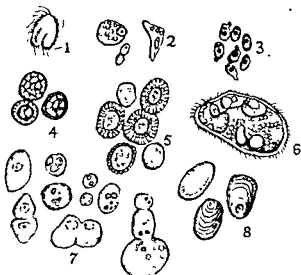


Fig. 101.—Objects in fæces likely to be mistaken for amœbæ or cysts.

1, Fatty acids (peculiar form) 2, Mucous cells 3, Yeast cells. 4, Spores of fungus 5, Cells from peas 6 Parenchyma cell of bean 7, Macrophage and other intestinal cells 8, Starch granules.

bottom, while the bulk consists of fæcal suspension containing the cysts. The

is washed several times by shaking up with tapwater and centrifugalizing. Finally the deposit is transferred to a slide, mixed with iodine solution and examined under the ⅙ in.-objective

Bacteriological Examination of Fæces

For dysentery bacilli.—If the stool is composed of blood and mucus

upside down with the top portion of the plate overhanging the bottom so to allow a current of air to pass They are then put out to dry Without dis [illegible]

but usually one is sufficient

If the stool contains fæces, as well as the blood and mucus, a portion of the latter is removed, washed in sterile normal saline, and transferred to a second [illegible]

loopful of the diarrhœic stool is transferred to the saline or peptone water tube and is treated as above It is essential to bear in mind that, even in the acute stages d [illegible] bacilli or [illegible] in small numbers in the exudate and [illegible]

other medium with a view to enriching the subsequent culture is contra-indicated

After spreading, the plate is incubated at 37 C for eighteen hours, by which time, Shiga or Flexner colonies become apparent as clear bluish grey droplets with a regular or slightly wavy margin, while Sonne colonies are irregular, the centres having a faint pink tinge where delayed fermentation [illegible]

[illegible]

four hours

sown on separate broth tubes and incubated for twelve hours The growth, which is scanty and tends towards opalescence (a heavy growth means that the organism is definitely not the dysentery bacillus), should then be examined microscopically, and subsequently tested out by means of biochemical and agglutination tests

Macroscopic agglutination tests -In order to perform this test an emulsion is made of the organism in 0 2 per cent formol saline solution, which should become distinctly opalescent It should then be dropped by means of a small-bore pipette into narrow glass agglutination tubes containing an equal

quantity of immune rabbit serum in various dilutions, for agglutination to occur

Garrow's agglutinometer is an instrument by which it is possible to recognize suspicious dysentery colonies on a plate by means of macroscopic agglutination Emulsions are made of the colonies in small quantities of formol saline and are then placed upon a glass slab and intimately mixed with an equal drop of a diluted Shiga, Flexner or Sonne serum in a dilution of 1 100

Considerations on which successful isolation of the dysentery bacillus depends —1. Period of the disease It is an accepted fact that dysentery bacilli are most numerous in the exudate in the early stages of the disease, but after the sixth day their isolation becomes a matter of increasing difficulty.

2 It is not possible to isolate the dysentery bacillus from every suitable stool at the first attempt This is especially the case with the stool of the very acute or fulminating forms of the disease which is passed early in such an attack and contains much dark and altered blood The author has frequently succeeded in isolating the bacillus on the second and third attempt.

3. Failure to isolate the bacillus from the stools does not necessarily indicate that it is not present in the intestinal canal of the patient. It is quite obvious that this is comparatively frequent It has been proved that the bacillus can be recovered at autopsy from the bases of chronic ulcers in the intestine in cases where a search during life has been vain.

4 The character of the cellular exudate may be taken as an index of the probability of successful culture Those stools which contain the largest number of undamaged pus-cells and red blood corpuscles and the fewest contaminating bacilli are the most favourable

5 Under tropical conditions the isolation of the dysentery bacillus can be made with great difficulty after the stools have been passed for four hours. It has been shown that stale specimens of stool become readily over-

[illegible]

pyocyaneus, which is a frequent concomitant. The difficulty of successful [illegible]

attempt.

Character of specimen	*Successful isolations*
Fresh, gelatinous, blood stained mucus Cellular exudate, fresh pus-cells, red cells, and few visible bacilli	73 3 per cent
Glairy mucus No blood Cellular exudate, pus-cells, and macrophages	62 5 ,, ,,
Blood and mucus Disintegrating pus-cells and numerous motile bacilli	41 8 ,, ,,
Bile-stained blood and mucus Disintegrating bile-stained pus-cells, and red cells	33 0 ,, ,,
Blood and mucus flakes intermingled with fæces	36 7 ,, ,,

Isolation of bacilli from carriers —This procedure should be carried out in the same manner as for carriers of the typhoid group In order to test speci-

mens satisfactorily, at least five platings are necessary and the fæces should be collected on a sterile swab The minute portions of fæces so removed should then be thoroughly emulsified in 5 c c of sterile saline and spread in a spiral manner on a suitable plate, using progressively smaller quantities of the emulsion for each successive plate

Isolation of the dysentery bacillus post mortem —The bacillus can be isolated with comparative ease from the early lesions of bacillary dysentery in the [illegible]

[illegible]

It has been recorded that dysentery bacilli may be isolated from the mesenteric glands and occasionally from the blood-stream, but this is by no means common

Viability of the dysentery bacillus —Fletcher and Jepps have made direct [illegible]

[illegible]

dysentery bacilli from the stools, 68 per cent positive results were obtained in the first five days, 17 4 per cent on the sixth to tenth days, and 6 3 per cent on the eleventh to thirteenth days

[illegible]

quantity of immune rabbit serum in various dilutions, for agglutination to occur.

Garrow's agglutinometer is an instrument by which it is possible to recognize suspicious dysentery colonies on a plate by means of macroscopic agglutination. Emulsions are made of the colonies in small quantities of formol saline and are then placed upon a glass slab and intimately mixed with an equal drop of a diluted Shiga, Flexner or Sonne serum in a dilution of 1 : 100.

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[illegible] The difficulty of successful [illegible]

attempt

Character of specimen	*Successful isolations*
Fresh, gelatinous, blood stained mucus. Cellular exudate, fresh pus-cells, red cells, and few visible bacilli	73.3 per cent
Glairy mucus. No blood. Cellular exudate, pus cells, and macrophages	62.5 „ „
Blood and mucus. Disintegrating pus-cells and numerous motile bacilli	41.8 „ „
Bile-stained blood and mucus. Disintegrating bile-stained pus-cells, and red cells	33.0 „ „
[illegible]	[illegible]

Antigenically Schmitz's bacillus and Shiga's bacillus are easily distinguishable Sonne's bacillus is antigenically homogeneous, while *B. dispar* appears to be antigenically heterogeneous

Schmitz' bacillus (*Bacterium ambiguus*) —This organism was first described in 1917 by Schmitz ; it was accepted as a dysentery bacillus by Kruse,

asylum infections It has been recovered post mortem from dysenteric

were recognized and five homologous sera were prepared , and for the general recognition of the Flexner group, a pooled serum of the combined strains was generally employed, but now this basis of recognition has been considerably amplified and modified by J S K Boyd (1940) who found considerable antigenic variation amongst the mannite fermenting group He collected 7,339 strains of dysentery bacilli from the military laboratories in India from 1932–35 Of these 14 3 per cent were Shiga, 5 5 per cent Schmitz, 10 9 Sonne, 50 2 per cent Flexner, 15 3 per cent definite lactose fermenters

in cats, dogs, rabbits, or monkeys, by injection, either per os or per rectum, with any members of the dysentery group

Sonne's bacillus

* It has been pointed out on several occasions that, strictly speaking, the organism should be known as the Sonne-Duval bacillus

ISOLATION OF THE DYSENTERY BACILLUS FROM HOUSE-FLIES

The following technique for the isolation of the dysentery bacillus from house-flies was adopted by the author in Fiji Four to six flies were caught on dysentery patients or in the dysentery ward. They were chloroformed and dropped into a tube of sterile saline

In any further work undertaken upon the carriage of dysentery bacilli by house flies, it must be borne in mind that, as pointed out originally by Graham-Smith, many non-lactose-fermenting bacilli found in the intestines of flies are indistinguishable culturally from *B dysenteriæ.*

DESCRIPTION OF DYSENTERY BACILLI

col

the

described by several workers As with other members of the *Bacterium* group, the antigenic structure is of far more importance in defining smooth and rough types than is the appearance of the colonies. The members of this group are not specially resistant, they are killed by a temperature of 55° C for one hour, or by 0 5 per cent phenol in six hours and 1 per cent. phenol in fifteen to thirty minutes They can resist drying for twenty to twenty-five days Dysentery bacilli are aerobes and facultative anaërobes, and the optimum temperature is 37° C With the possible exception of *B alkalescens*, none appear to be capable of producing an active hæmolysin against sheep cells

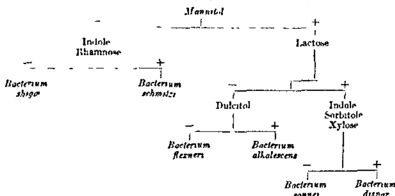
B. shigæ and *B schmitzi* produce acid from glucose, but the remaining

alkalinity

serum has some agglutinating action on some strains of the Flexner group.

TABLE XX

CLASSIFICATION OF BACTERIA OF THE DYSENTERY GROUP
(After W. W. C Topley and G. S Wilson)



bacillus The term pseudo-dysentery bacillus does not find favour in modern bacteriological circles. In 1904 the bacillus appears to have been rediscovered by Duval and then again a few years later, in 1912, by K. Baerthlein, who recovered it in a dysentery like epidemic in Berlin. In 1915 C Sonne gave a detailed description of this organism during a similar epidemic

[illegible]

organism in Rio de Janiero, and R. I. Nelson has found it widespread in children in Boston In Japan it gives rise to acute dysentery in children known as " Ekiri "

Originally the Flexner organism, Sonne's bacillus, and Schmitz's bacillus were included under the name *Bacillus pseudodysenteriæ* This classification is not used in England, as Flexner infections of great virulence have been reported, and in 1933 it has been shown that the toxins of Sonne's bacillus can cause virulent symptoms simulating food-poisoning It is closely related to *B dispar* (Table XX)

Sonne's bacillus is non-motile, and in morphological characters resembles members of the Flexner group, colonies on gelatin and agar plates also resemble these organisms W R Wiseman (1927) has pointed out the tendency of this organism to bipolar staining It is capable of fermenting *lactose jelly. On agar, two forms of colonies are found, one round and smooth,* the other flat and irregular On lactose-litmus agar, colonies are at first bluish, and later reddish, no indole is produced Litmus milk remains

[illegible]

It will be noted that the final volume of fluid in each tube, when the bacillary emulsions are added, is twenty five drops By calculation it will be seen that in tube 1 of each row the serum acts in a dilution of 1 25

In tube 2	in a dilution of	1		125
,, 3	,,	,,	1	500
,, 4	,,	,,	1	1,000

The tubes are examined after four hours at 37 C, or two hours at 50°-55° C, followed by fifteen minutes at room temperature The reading is taken by comparing each tube in succession with the control tube, and is

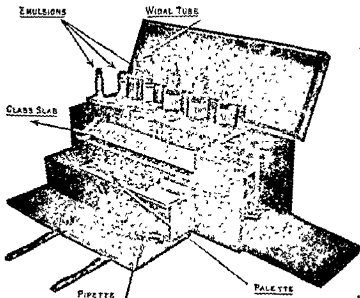


Fig. 102 —Garrow's agglutinometer, showing instrument ready for use *

preferably made by means of artificial light against a black background If daylight is used, the tubes should be partly shadowed by passing a finger up and down behind them

Rapid method of macroscopic agglutination by Garrow s agglutinometer (Fig 102)—This is a practical method suitable for small laboratories, and is based upon the slide method of agglutination originally described by Broughton Alcock It may be used for recognition of pathogenic bacteria isolated from the blood or excreta by means of specially prepared serums Macroscopic agglutination becomes visible in as short a period as three minutes, no incubator is needed

* This instrument can be obtained from Messrs Baird and Tatlock, Ltd Cross Street, Hatton Garden, London E C 1

for which standardized bacillary emulsions can be obtained The standard culture is as sensitive to agglutination as is the fresh culture; it is, moreover, sterile and, if stored in a cool, dark place, can be kept indefinitely.

quently with absolute alcohol and ether, so as to dry thoroughly. Take up the serum to be tested into the dried pipette. Measure out six drops of the serum into the dilution tube already containing the fifty-four drops of saline, thus obtaining a dilution of 1 : 10

Thus —

① ② ③ ④ ⑤ ① ② ③ ④ ⑤ ① ② ③ ④ ⑤

S	F	So
15 drops	15 drops	15 drops

For the addition of the diluted serum it is best to commence with higher dilutions before proceeding to the lower ones To tube 3 in each row add ten drops of 1 : 200 serum, to tube 4 in each row add five drops of 1 : 200, to tube 1 add ten drops of 1 : 10 dilution, and to tube 2 also add two drops of 1 : 10 dilution The pipettes must be washed out before proceeding to add the saline The addition of saline should then be made to tubes 2 and 4, which receive eight and five drops respectively, while tube 5 receives no serum, but ten drops of saline only, and acts as a control against spontaneous agglutination This can be best represented by the following scheme —

No of tube	*Drops of normal saline*	*Drops of serum* Dilution of 1 · 10
1	0	10
2	8	2
		Dilution of 1 : 200
3	0	10
4	5	5
5	10	0

drops

cleansing with alcohol, and (3) drying with ether It is a good plan to keep a piece of old linen specially for this purpose In cold weather the drops can be made to run more freely by gently heating the slab before use, or by breath-

emulsion

Fig 106 shows the appearance of the slab after carrying out the above process

Dilutions of serum

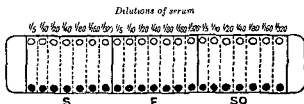


Fig 106 —Slab with bacillary emulsions and dilutions of serum

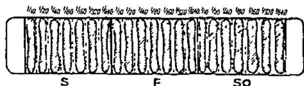


Fig. 107 —Intermingling of serum and emulsions

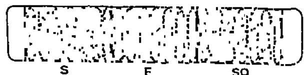


Fig 108 —Reaction complete, showing appearance of agglutination in S and SO.

S = Shiga, F = Flexner, SO = Sonne

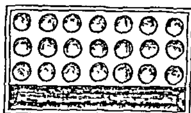


Fig 103.—"Palette" for diluting serum, used with the agglutinometer.

fitting Morse gauge No 70 is the correct size)—*that is,* when mingled with an equal quantity of bacterial emulsion, it should not run over the edge of the glass slab (Fig 104) (3) The *agglutinometer slab,* a piece of plate glass 11¾ in long by 1¼ in wide, divided into a number of partitions by double grooves running at regular intervals of 1 cm in order to prevent the dilutions from intermingling (Fig 106) (4) *Set of bacterial emulsions* The stock

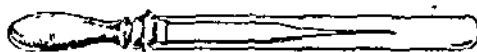


Fig. 104.—Drop pipette used with the agglutinometer.

saline The emulsions should be very dense, of milky consistence and uniform suspension

In order to promote the intimate mixture of the serum under investigation and the bacterial emulsions, the slab is made to revolve by clock-work at a uniform rate of about fifteen revolutions per minute. For field use the slab may be placed in a simple box provided with damp blotting-paper in order to obviate desiccation, and turned by hand with a handle attached to a wooden shaft which supports the glass slab.

The diluting process —The blood for examination is taken from the finger and collected in a capsule Three large drops of blood are sufficient; the ends of the tube are sealed with wax or plasticine (Fig 105) After stand-



Fig. 105.—Special straight capillary tube for collecting serum.

ing for some time the serum separates, rendering centrifugalization unnecessary. By means of the pipette, two drops of clear serum are abstracted and placed in the first partition of the mixing palette In order to make a dilution of 1 . 5, eight similar drops of normal saline are added From the

Isolation of the cholera vibrio from fæces.—For the isolation of the cholera vibrio, a loopful of the suspected stool is inoculated into peptone

and are incubated overnight at 37° C The peptone culture is returned to the incubator and in twelve to twenty-four hours is tested for the cholera red reaction This consists of adding three to five drops of concentrated pure sulphuric acid to the culture when, if positive, a rose red colour develops Some brands of peptone inhibit the reaction, and in some instances the reaction is positive only when there is a pure culture of the vibrio After incubation the plates are examined for typical colonies of the organism and agglutination tests are performed

The colonies emulsify with great ease A simple and rapid method is to make two vaseline circles side by side on a microscopic slide Inside one ring is placed a loopful of normal saline and in the other a loopful of 1 500 cholera serum , to each is now added a loopful of a saline emulsion of one of the suspected colonies The circles are covered with cover glasses and examination is made under the low power of the microscope The diluted serum preparation, if positive, quickly shows absence of motility and curdy agglutination, while the other remains uniformly turbid and shows motility.

Isolation of the tubercle bacillus from fæces.—Baldwin, Petroff

allowed to stand at room temperature for several hours At the end of this time the bacteria will have floated to the surface and the scum can be collected with a sterile spoon and transferred to a clean wide mouthed bottle Two volumes of normal caustic soda are added and the mixture is well shaken and incubated for one to two hours at 37° C The specimen is now centrifugalized, the clear fluid decanted, and three or four drops of normal HCl are added to the deposit The sediment may be divided into three portions, one for staining, one for inoculation into suitable media, and the third for animal inoculation It must be borne in mind that not all acid fast bacilli found in fæces are tubercle bacilli, it has been repeatedly demonstrated that non pathogenic acid-fast organisms may be present

Pappenheim's stain for tubercle bacilli —This method is employed to safeguard against confusing *B smegma* and other acid-fast bacteria with the

The slide so prepared is placed in the moist chamber of the ...

to and fro across the slide. At the end of three minutes the clockwork is

...

nostic significance is present in the blood

Fig 108 shows the appearance of the agglutinometer slide in the case of a patient whose blood agglutinates S up to 1 : 320, SO up to 1 : 160, the Flexner emulsion being negative

Agglutination Tests

An emulsion of a pure culture of the organism is made in saline and tested on the agglutinometer, or in tubes, against specific serums. In routine examinations it is convenient to keep the stock dilution of the serum (say

...

is heat-stable

quantity of infected mucus or fæces The material is inoculated into the bottom of the tube with the aid of a wide-bore pipette, and the tubes are incubated at 37° C. Cultures may be examined twenty-four hours later, when material is removed from the bottom of the tube by means of a pipette It is advisable to scrape the surface of the egg or serum slope with the pipette to remove adherent amœbæ before sucking up a sample Sub-cultures should be made every four to six days When rice starch has been added, it will be found that amœbæ have ingested the smaller particles Cysts may be produced

2. For the cultivation of intestinal flagellates.

Tanabe's medium.—This is prepared by mixing —

Sodium chloride	0 7	grm
Sodium citrate	1 0	grm
Distilled water	100	c c

Sterilize in the autoclave or by boiling, and when cool add 0 5 gramme of Loeffler's dehydrated blood-serum and 2 c c of whipped white of a hen's egg, prepared as aseptically as possible Fill into test-tubes, about 10 c c to each [illegible]

Agar	15	grm
Sodium chloride	6	grm
Distilled water	900	c c

Steam [illegible]

the aid of a long, wide bore pipette

Most of the intestinal flagellates (but not *Giardia* (*Lamblia*) *intestinalis*) have been cultivated on this medium It has also been used successfully for cultivation of *Balantidium coli*

Selective Media for the Isolation of Organisms of the Dysentery Typhoid Group

McConkey's bile salt lactose agar —To 1,000 c c of distilled water in a flask is added —

Agar powder	25	grm
Peptone	20	grm
Sodium taurocolate	5	grm

Mix thoroughly and steam at 100° C for two hours Cool to about 60° C and adjust reaction to *p*H 7 8–8 0 Add the well-whipped whites of two eggs and return to the steamer to clear Filter through thick Chardine filter paper Add 10 grammes of lactose and 2 5 c c of a 1 per cent. watery solution of neutral red Tube off, about 10 c c to each tube, and sterilize for thirty minutes at 100° C on three successive days

On this medium *B coli* colonies are bright pink, streptococcal colonies small and deep red, and colonies of *B dysenteriæ* and *B typhosus* bluish-grey "dew-drop"

CULTURE MEDIA FOR INTESTINAL PROTOZOA

1. For the cultivation of amœbæ.

Boeck and Drbohlav's medium (L.E.S.)—Four hens' eggs are washed in water, wiped with alcohol and broken into a sterile, wide-mouthed, stoppered *bottle containing glass beads Fifty c c. of Locke's solution are added and* the bottle is well shaken to effect solution Test-tubes are filled with a sufficient quantity to produce slopes one and a half inches long, slanted in an inspissator and heated to 60° C. for one hour On the second day the tubes are again inspissated at 60° C. for one hour, and on the third the temperature

Berkefeld filter (No N) once or twice to remove contaminating bacteria When sterile it is further diluted with Locke's solution to bring the dilution to 1 8.

LOCKE'S SOLUTION

Sodium chloride	9 0	grm.
Calcium chloride	0 24	grm
Potassium chloride	0.42	grm.
Sodium bicarbonate	0 2	grm
Glucose	2 5	grm
Distilled water	1,000	c c

The best growth of amœbæ occurs when the reaction of the medium is between pH 7 2 and 7 8

Boeck and Drbohlav's medium (L E A.)—A modification of Boeck and

the liquid, together with powdered rice starch To prepare the medium, suitable volumes of horse serum, sterilized by filtration, are placed in tubes with aseptic precautions, and inspissated at 80° C for one hour It is important not to over heat the serum Ringer's solution, containing the whipped whites of four eggs per litre and previously sterilized by filtration through a candle filter, is now added to the top of the column in each tube

RINGER'S SOLUTION

Sodium chloride	9 0	grm
Potassium chloride	0 2	grm
Calcium chloride	0 2	grm
Distilled water	1,000	c c

in 100 c c amounts and sterilize by free steam (and up to 5 lbs) for one hour
Prepare —

Solution A		Solution B	
Sodium citrate	17 grm	Sodium desoxycholate	10 grm
Sodium thiosulphate	17 grm	Distilled water	100 c c
Ferric citrate	2 grm		
Distilled water	100 c c		

These solutions need not be sterilized

[illegible]

The medium is pale and slightly opaque *B sonnei* colonies are round, about 2 mm in diameter, with a well defined edge and no appearance of "roughness" They may be pale pink, or become so on further incubation or storage *B flexneri* colonies are similar, but may have a narrow plane periphery surrounding a central zone *Paratyphosus B* colonies are larger, 2–4 mm in diameter, often with a black central dot Salmonella colonies are similar, and those of *B typhosus* are flat and round (M Haynes, 1942)

Teague's medium —To distilled water in a flask is added —

Agar powder	15–30	grm
Peptone	10	grm
Sodium chloride	5	grm
Meat extract (Lemco)	5	grm

Mix thoroughly and steam at 100° C for two hours Cool, add the well-whipped whites of two eggs, and return to steamer to clear Filter through Chardine filter paper Adjust the reaction to pH 7 8, then add —

Saccharose	5	grm
Lactose	5	grm

The medium is flasked off in 50 c c amounts, is sterilized for half an hour on three successive days, and is stored in an ice-chest When required for use it is melted, and to each 50 c c is added 1 c c of 2 per cent yellowish eosin and 1 c c of 0 5 per cent methylene blue Mix thoroughly, pour plates, and allow to dry off

On this medium, after eighteen hours, *B coli* colonies are deep black and opaque, and *B. dysenteriæ* and *B typhosus* are colourless and transparent

WILSON AND BLAIR'S MEDIUM (MODIFIED) FOR THE ISOLATION OF B TYPHOSUS AND B PARATYPHOSUS B

[illegible]

Conradi-Drigalski medium.—To 1,000 c.c. of distilled water in a flask is added :—

Peptone	10	grm.
Nutrose	10	grm.
Sodium chloride	5	grm.
Meat extract (Lemco)	5	grm.

days.

On this medium *B. coli* colonies are pink and those of the dysentery-typhoid group bluish-grey and transparent.

Endo's medium (fuchsin agar).—To 1,000 c.c. of distilled water in a flask add :—

Powdered agar	30	grm.
Peptone	10	grm.
Meat extract (Lemco)	5	grm.

Mix thoroughly and steam at 100° C. for two hours. Cool to about 60° C. and adjust the reaction to *p*H 7.8–8.0. Add the whipped whites of two eggs and

Chemically pure lactose	1 grm.
10 per cent. alcoholic solution of basic fuchsin	0.5 c.c.
Anhydrous sodium sulphite	0.125 grm.

The sodium sulphite is dissolved in a small quantity of hot, sterile distilled water and is made up fresh each time.

Mix thoroughly, pour plates, and allow to harden in the incubator before "sowing."

On this medium *B. coli* colonies are vermilion, streptococcal colonies deep red, and *B. dysenteriæ* and *B. typhosus* greyish.

LEIFSON'S DESOXYCHOLATE-CITRATE MEDIUM. (HAYNES' MODIFICATION.)

in 100 c c amounts and sterilize by free steam (and up to 5 lbs) for one hour

Prepare —

Solution A		Solution B	
Sodium citrate	17 grm	Sodium desoxycholate	10 grm
Sodium thiosulphate	17 grm	Distilled water	100 c c
Ferric citrate	2 grm		
Distilled water	100 c c		

These solutions need not be sterilized

For use —Melt 100 c c of the agar base and add 5 c c each of solutions A and B in this order, using separate pipettes and mixing well between Pour plates immediately and dry the surface Inoculate plates heavily and incubate for 24 hours A further 24 hours' incubation may be necessary

[illegible] e larger, 2–4 mm [illegible] olonies are similar, [illegible] 942) [illegible] —

Agar powder	15–30	grm
Peptone	10	grm
Sodium chloride	5	grm
Meat extract (Lemco)	5	grm

Mix thoroughly and steam at 100° C for two hours Cool, add the well whipped whites of two eggs, and return to steamer to clear Filter through Chardine filter paper Adjust the reaction to pH 7 8, then add —

Saccharose	5	grm
Lactose	5	grm

[illegible]

to dry off

On this medium, after eighteen hours, *B coli* colonies are deep black and opaque, and *B dysenteriæ* and *B typhosus* are colourless and transparent

WILSON AND BLAIR'S MEDIUM (MODIFIED) FOR THE ISOLATION OF B TYPHOSUS AND B PARATYPHOSUS B

Difco dehydrated Wilson and Blair's medium powder (Difco Laboratories), [illegible]

[illegible] hours incubation are round, about 2 mm in diameter, jet black,

and surrounded by a blackish zone, which has an intense metallic sheen in

instances, only well-separated colonies are black, so the method of spreading should ensure that colonies are well-separated Other Salmonella may resemble *B. paratyphosus B*, or the colonies may not blacken but remain dark green (M Haynes, 1942)

Selective Media for the Isolation of V. Choleræ

Dieudonné's blood alkali agar—Equal parts of defibrinated ox-blood and normal caustic-soda solution are mixed and sterilized in a steamer at 100° C for thirty minutes on three successive days. When required for use, 30 c c are mixed with 70 c.c. of melted nutrient agar Plates are poured and are kept at 60° C. for thirty minutes; they are left half open in the incubator overnight for the ammonia to vaporize Organisms other than cholera and cholera-like vibrios will not develop on this medium.

Esch's medium.—500 grammes of minced lean beef are mixed with 250 c c. of normal caustic-soda solution in a clean enamel saucepan The mixture is simmered for two or three hours, filtered, and sterilized One part of this alkaline extract is added to two parts of nutrient agar. The transparency of this medium aids the identification of cholera colonies, which are bluish-grey and transparent

Aronson's medium—To 100 c c. of 3 per cent. nutrient agar add 6 c c. of a 10 per cent. solution of desiccated sodium carbonate, and steam for fifteen minutes. Add 5 c.c of a 20 per cent. watery solution of saccharose, 5 c c. of a 20 per cent watery solution of dextrin, 0.4 c.c of a saturated alcoholic solution of basic fuchsin, and 2 c c of a 10 per cent. watery solution of sodium sulphite A precipitate forms which quickly settles. Plates are poured from the supernatant fluid. Cholera colonies develop in twelve hours and show as red colonies in fifteen to twenty-four hours. *B. coli* colonies are much larger than cholera and are colourless.

Bismuth Sulphite Media for the Isolation of V. choleræ (Wilson and Blair modified)

Fluid medium—(a) To 100 c c. boiling water add anhydrous sodium [illegible] bismuth ammonio-citrate scales

[illegible] icose, saccharose, mannitol

[illegible] Cool and mix the selected

[illegible] which will have a pH of

[illegible]

The m

dysenter

vibrios,

organism

characteristic colonies

STAINING METHODS

Heidenhain's iron hæmatoxylin —For amœbæ, flagellates, and cysts in fæcal smears

1 *Fixing solution* (Schaudinn's Fluid)—Absolute alcohol, one part, saturated watery solution of corrosive sublimate, two parts Add

Method—(a) Prepare thin films, thinning the fæces with normal saline

alcohol to water

(g) Transfer to mordant (2) and leave six to twelve hours Rinse rapidly in water

(h) Tr [...] velve hours till

control under

(j) Wash in several changes of water, then in alcohols 30 per cent, 50 per cent, 90 per cent to absolute alcohol, equal parts absolute alcohol and xylol, xylol two changes, and finally mount in neutral Canada balsam.

Phosphotungstic acid hæmatoxylin.—For amœbæ and flagellates. (Not for cysts)

Thin smears of fæces are made on cover-glasses If firm, the fæces are first emulsified with normal saline

fifteen minutes and wash again in water.

(d) Transfer to water in which one crystal of hyposulphite of soda ("hypo") has been dissolved, leave till brown colour has disappeared, and wash in water

(e) Pour on phosphotungstic acid hæmatoxylin and leave covered on laboratory bench overnight (twelve hours) Differentiate in running water.

(f) Wash in absolute alcohol (twice), absolute alcohol and xylol equal parts, and xylol (twice) Mount in Canada balsam.

Differentiation should not be prolonged (one minute) and the films should not be left for any length of time in the alcohols If overstained take out excess of stain very quickly with 0 5 per cent acid alcohol and wash in water before proceeding through alcohols.

To prepare the stain.—Hæmatoxylin 1 gramme is dissolved by heat over

Although cysts are stained well by this method, for some unknown reason they burst after a day or two, and the slides are quite useless as permanent preparations

Heidenhain's iron-hæmatoxylin.—For paraffin sections

Tissues are fixed in Zenker's fluid which is made as follows —

Potassium bichromate	2.5 grm
Sodium sulphate	1 grm
Corrosive sublimate (mercuric chloride)	5 grm.
Distilled water	100 c c
To this stock solution is added, before use, acetic acid	5 c c

They are fixed for several days, depending on size of the tissue, are washed in running water for twelve to twenty-four hours, and are preserved in

mounted and are treated as follows —

(a) Remove paraffin with xylol
(b) Remove xylol with absolute alcohol.
(c) Wash in 70 per cent alcohol
(d) Place in 70 per cent alcohol containing a small quantity of iodine solution to remove mercury
(e) Wash in water

ur

(i) Wash in water.
(j) Differentiate under microscope with 1 per cent iron alum solution.
(k) Wash in water.
(l) Wash in 70 per cent alcohol

[illegible]

To obtain the best results it is necessary to follow the method step by step. Sections cannot be hurried through and at no stage may they be allowed to dry

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(*See also Sonne Dysentery*)

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Philipp J Sci, 22, 1
Med, 4, No 3, 309–30
[illegible] 5) J. Trop Med (Hyg), 24, 289
[illegible] o 2, 67
[illegible] h, 22, 315
[illegible] testinal Protozoa in the Near East London

INDEX

A

INDEX

A

C

E

I

J

K

W

X

Y

Z

